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THE BLOOD PRESSURE OF ADOLESCENTS

Observations on Two Hundred and Twenty Students

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DURING the routine annual examination of 220 healthy male and female adolescent students, I was impressed with the frequency with which the blood-pressure readings reached elevated levels. In many cases, rapid pulse, excessive perspiration, vasomotor phenomena and other signs of excitement were absent. It was therefore decided to make further observations on these subjects, to compare the incidence of abnormal pressures with that in a group of young adults and, where possible, to obtain information regarding the blood pressures of the parents.

NORMAL BLOOD PRESSURES OF ADOLESCENTS

Before classifying a given blood-pressure reading as abnormal, it is necessary to know the normal reading for persons of the same sex and age. The blood pressure of adolescents should not be judged by adult standards. It has been pointed out that the blood pressures of normal children of the same age vary within wide limits, and that the normal value may be best described as a range.[1]

The only studies of the blood pressure of sizable numbers of children available to me are those of Richey,[1] Faber and James,[2] Schnurman[3] and Sundal.[4] Sundal recorded only the systolic pressures obtained by the method of palpation. Schnurman did not observe persons below the age of seventeen. Faber and James did not record readings on adolescents older than sixteen. Consequently, the values given by Richey are the only ones suitable for the purpose of this study. The mean pressures and standard deviations recorded by him on students of the same age and racial stock as those observed in this study are given in Table 1.

In order to determine whether a given blood-pressure reading is normal, use is made of the statistical method of frequency distribution. This method is explained by Faber and James[2] as follows: the nearer the pressure of a given subject is to the average of all normal persons, the greater is the chance that his pressure is normal; and the greater the deviation from the average, the greater the chance that his pressure is abnormal. The proportions are determined in the statistical system by the use of a measure of deviation from the mean, or average, which is known as the "standard deviation" (the square root of the arithmetical mean of the squares of the deviations from the average of the distribution). By dividing the deviation of a given measurement from the average by the standard deviation, one obtains a quotient, called by Faber and James the "deviation index." This index is of clinical value in determining the significance of individual variations.

TABLE 1. *Blood Pressures and Standard Deviations in Adolescents (Richey[1]).*

	Age	No. of Cases	Mean Systolic Pressures	Mean Systolic Standard Deviation	Mean Diastolic Pressures	Mean Diastolic Standard Deviation
	yr.		*mm. Hg.*	*mm. Hg.*	*mm. Hg.*	*mm. Hg.*
BOYS						
	14	112	106.36±0.66	10.37±0.47	64.14±0.52	8.22±0.37
	15	133	110.28±0.65	11.16±0.46	66.04±0.42	7.11±0.29
	16	145	111.99±0.57	10.22±0.40	66.34±0.48	8.50±0.34
	17	112	111.68±0.64	10.06±0.45	67.43±0.54	8.42±0.38
	18	43	112.77±1.13	11.02±0.80	68.95±0.86	8.38±0.61
	19	13	117.00±2.68	14.35±1.90	68.85±1.54	8.24±1.09
GIRLS						
	14	115	103.94±0.65	10.27±0.46	67.10±0.48	7.65±0.34
	15	121	105.88±0.63	10.31±0.45	67.43±0.45	7.36±0.32
	16	128	106.69±0.63	10.53±0.44	69.09±0.45	7.50±0.32
	17	97	102.96±0.63	9.94±0.48	66.88±0.54	7.52±0.36
	18	34	100.53±1.18	10.22±0.48	66.41±1.05	9.06±0.74
	19	7	104.71		66.43	

METHOD OF STUDY

The blood pressure of each student was taken at the time of his or her annual examination, a single reading being recorded. These readings were compared with Richey's[1] statistics for adoles-

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cents of the same sex and age. All subjects whose deviation indices were + 2.00 or more were recalled for a second examination. This dividing line is purely arbitrary; so are the criteria for classifying adult pressures as normal or otherwise. It should be noted that a deviation index of + 2.00 indicates that the odds against that reading's being normal are 1 to 43.[2] In a series of ideally distributed normal cases only 2.3 per cent will have indices of + 2.00 or higher.

Blood-pressure readings were made by a standard method[5] by one or both of two observers, whose readings were found in preliminary tests to check closely. Beginning with this second observation, the average of three or more readings was taken as the true reading. On the students whose deviation indices remained + 2.00 or above, still further readings were made, including cold-pressor tests. In addition, information regarding the incidence of elevated blood pressure in the parents was sought.

TABLE 2. *Data on 21 Subjects with Continued Blood Pressures of a Standard-Deviation Index of + 2.00 or More.*

Case No.	Sex	Age	Range of Blood Pressure*	Cold Pressor Test			Blood Pressures of Parents
				Basal	Response	Time for return to basal response	
		yr.	mm. Hg.	mm. Hg.	mm. Hg.	min.	
1	F	17	122–130/80–90	114/68	130/104	3	"No known hypertension"
2	F	15	120–150/70–80	118/70	134/100	3	"No known hypertension"
3	M	18	138–150/60–70	128/70	140/88	3	"No known hypertension"
4	M	17	136–152/76–98	128/80	146/104	2	"No known hypertension"
5	M	17	128–148/70–80	120/74	138/100	1	Father: hypertensive invalid Mother: pressure unknown
6	M	17	130–148/60–80	136/68	148/90	3	Father: pressure unknown Mother: 136/80
7	F	18	124–142/64–70	114/64	128/90	3	Father: pressure "slightly high" Mother: pressure unknown
8	M	19	130–140/80–86	120/70	134/98	3	Father: 130–180/80 Mother: 130/?
9	M	18	112–140/70–82	110/70	112/80	1	Father: 116/66 Mother: 142/76
10	F	17	136–142/76–80	130/80	144/90	2	Father: died of hypertension Mother: pressure unknown
11	F	17	122–140/68–80	138/80	140/98	1	Father: pressure unknown Mother: 136/76
12	F	18	122–142/68–80	126/82	136/90	2	Father: died of tuberculosis Mother: 158/76
13	F	16	118–132/72–74	114/70	130/100	3	"No known hypertension"
14	F	17	116–126/80–90	114/76	124/100	2	No information
15	F	17	126–144/70–84	112/60	130/90	1	Father: pressure unknown Mother: 148/84
16	F	18	130–150/68–80	130/70	130/84	1	Father: pressure unknown Mother: 138/84
17	F	15	126–142/58–80	112/78	126/90	4	Father: died of hypertension Mother: 162/90
18	M	17	134–152/72–76	130/70	140/110	4	Father: died of septicemia Mother: pressure unknown
19	M	14	130–140/68–78	124/70	134/98	2	Father: 130/80 Mother: 164/106
20	M	17	134–140/60–66	126/80	134/100	2	Father: 130/80 Mother: 170/100
21	M	15	150–158/70–80	148/80	162/90	1	Father: pressure unknown Mother: 180/100

*These figures indicate the lowest and highest values recorded in three or more observations some days or weeks apart; the readings are given in nearest even numbers.

Results

Of the 220 students initially examined, 82, or 37 per cent, exhibited blood pressures whose deviation indices were + 2.00 or more. Obviously, many of the elevated readings were due to excitement, although only 13 of the 82 subjects exhibited pulse rates of 90 or above. This was made further apparent by the second observation, when only 21, or 9.5 per cent of the entire series, continued to have elevations in blood pressure of this degree.

All the subjects had high systolic levels on more than one occasion. Cases 1, 9 and 14 had elevated diastolic levels as well. There is evidence that diastolic elevations are more significant than systolic.

The cold-pressor test was done on each of these 21 subjects according to the technic described by Hines.[6] The subject was placed at rest in a reclining position in a quiet room, and the blood pressure was taken every ten minutes until a basal level was reached. The hand was then placed in ice water up to the wrist, and the blood pressure was read on the opposite arm after thirty seconds and after sixty seconds. The hand was then removed from the water, and readings were taken every minute until the basal level was regained. An abnormal response, according to Hines, consists of an elevation of 20 mm. or more in the systolic reading, an elevation of 15 mm. or more in the diastolic reading or failure to return to the basal level within two minutes. The diastolic response is said to be a more reliable index of vasoconstriction than the systolic. Among this group there were no students with excessive systolic responses. However, 16 of the 21 subjects, or 7.3 per cent of the entire series, showed diastolic responses of 15 mm. or more; and 10 of the 16 showed delay in returning to the basal level. This incidence of abnormal reactions should be compared with the 18.7 per cent incidence of hyper-reactors found by Hines[7] among 400 school children.

Blood Pressures of Parents

In 11 of the families of the 21 students with abnormally high pressures, the blood pressures of one or both parents were measured by me. In 5 couples, one parent had a systolic pressure greater than 150; and in 2 others, the systolic pressures were 142 and 148 in one of the parents. Furthermore, the husband of a hypertensive mother had died of hypertension. Unfortunately, it was impossible to observe any parent on more than one occasion.

The parents of 9 students gave what information they had by letter. One father had died of the complications of hypertension; the father of another was said to be a hypertensive invalid; and the father of still another had a "slightly high" blood pressure. There was no known hypertension in the remaining 6 couples.

Thus, in 20 couples concerning whom information was available, hypertension is known to be or to have been present in 7, and possibly in 10.

Comment

The incidence of hypertension among Selective Service registrants is said to be 3.02 per cent.[8] Yet in the present study, the blood pressures of 21 of 220 adolescents, or 9.5 per cent, after repeated examinations were not considered normal. This may be explained in three ways: first, because Selective Service examiners do not determine abnormality by the method of frequency distribution, as was done in this group; secondly, because at least some examiners for the Selective Service System have subjects lie down if the initial reading is elevated, thus getting something comparable to the basal level of the cold-pressor test; and thirdly, because adolescents go through a period when they have elevated pressures that may become normal in young adult life, only to rise again to hypertensive levels in middle age.[9]

The hereditary aspects of hypertension have been pointed out repeatedly,[7, 10–13] so that no comment on this aspect of the present study is needed here.

Conclusions

The drawing of definite conclusions regarding blood pressure from such a small number of observations is not in order. However, the following statements seem justified:

Blood-pressure determination should be part of the examination of students, but only if the readings can be checked at one or more later dates, for the pressures of adolescents are labile.

A certain proportion of students — 9.5 per cent in this group — will show abnormally high pressures, as determined by the method of frequency distribution, after repeated observations. Most of these persons come from hypertensive families.

The frequency of abnormal pressor tests among these adolescents with abnormal pressures tends to confirm the impression that many of them are in a prehypertensive stage.

There is need for follow-up of subjects such as those described, in order to determine in later years whether elevated blood pressures and abnormal pressor tests during adolescence are truly indicative of a prehypertensive state.

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THE USE OF COAL TAR IN THE TREATMENT OF SKIN DISEASES*

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IN THE field of dermatology there probably exists no more valuable and useful remedy than crude coal tar. Nevertheless, no other substance in the *National Formulary* varies so in composition and consequently in pharmacologic action. This physical and chemical difference of coal tars derived from varied sources was originally emphasized by Dind,[1] who compared coal tars obtained from the gasworks of Lausanne, Geneva, Zurich and Basle. Brocq[2] recommended that one should insist on obtaining the coal tar produced in the making of illuminating gas. In these times it is impractical if not impossible to pursue such a policy. Many dermatologists when prescribing coal tar refer the patient to a certain pharmacist because the former knows the type of coal tar dispensed. If this is not practical, experience has shown that the patient not infrequently is given a mixture of uncertain composition, poorly compounded, which not only fails to benefit him but may be actually injurious. Furthermore, it is astonishing how often, when one prescribes pix carbonis, the pharmacist dispenses liquor carbonis detergens, a 20 per cent solution in an alcoholic soap-bark vehicle.

At the present day not only do the available coal tars differ from each other, but they all differ materially from that formerly recommended by Brocq, Jambon, Dind, Jadassohn and other European dermatologists. White,[3] who introduced the use of coal tar in this country, was the first American dermatologist to mention this difference. Schamberg[4] was so impressed with the unsatisfactory action and variability of the substance that he imported European tar for the use of his patients.

For a number of years at Bellevue Hospital, our experience has been similar to that in other sections of the country. Various lots of coal tar have differed in physical characteristics, color, consistence, homogeneity and therapeutic effect. On some occasions the substance used has been actually irritating. This difference is due not only to the crude tar itself but also to the method by which the paste is compounded. It is extremely difficult to prepare by hand a good paste in large quantities. The finished product should be smooth, homogeneous and almost black. This shade does not differ perceptibly in pastes containing from 3 to 10 per cent of crude tar. Inferior and unsatisfactory pastes are sometimes an olive green, often flecked with small black particles, and lack the characteristic naphthalene-like, gassy odor.

What are the reasons for these differences in coal tars from different sources? The coal tar used by the early European dermatologists was the residue from anthracite coal in the manufacture of illuminating gas (pix lithanthracis). There were few uses for the crude tar, other than as a paint for wood, iron, rope, roofing, brickwork or stone as a protection against weather and fungi. It was subsequently distilled solely for the purpose of obtaining naphtha, creosote and phenol. In more recent years the value of coal-tar distillation fractions has assumed such importance in the arts and in industry that the manufacture of illuminating gas must be considered secondary. The separation of its constituents became an industry much more important than all the applications of crude coal tar itself. It was found that with variation in the temperature of the coal ovens, the time of distillation, the type of oven (vertical or horizontal) and so forth, differences occurred in the type of tar produced; that is, certain fractions were increased or decreased in amount. Coal tar was subsequently produced, therefore, of a composition depending on what fraction was particularly desired. This explains in part why many manufacturers use petroleum oil, coke, splint coal, lignite and other carbonaceous material, although the tar is medically more valuable when materials other than real coal have been used.

The only solution to the coal-tar problem appeared to be that a good crude product should be obtained and a competent manufacturer desig-

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nated to prepare a good paste. This was done, the product* consisting of the following ingredients:

Crude coal tar	2.88
Zinc oxide	5.37
Starch	53.75
Petrolatum, q. s. ad	100.00

Method of Application

Detailed attention to the correct method of application and removal of coal-tar paste is essential to the best results.

All previous medication should be carefully removed by means of some fixed oil. The paste should then be applied directly by means of a wooden spatula in a layer just thick enough to cover the lesion. The entire area should then be dusted with talcum until the surface is white. If possible it is preferable not to cover the lesion with a dressing. If this cannot be avoided, the lightest type of dressing should suffice. The paste should remain undisturbed for at least twenty-four hours, and in some cases it may be left for two or three days.

Removal is best accomplished by using mineral oil or an emollient cream. No attempt should be made to cleanse the area completely; only the loose particles should be removed. A new layer of coal-tar paste is then applied in the manner previously described.

If papules appear on the treated area, the coal tar should be discontinued. They are the forerunners of pustules which may complicate therapy and are encouraged by too much bandage and a paste that is too thin.

Tar which has soiled linens and bedclothing may be readily removed by rubbing both sides of the material with lard and washing with soap and water.

The following precautions should be observed:

Avoid exposure to direct sunlight of the area to which tar is applied or has recently been applied. Tar is a photosensitizer, owing to the presence of acridine and anthracene oils.

Avoid prolonged use of tar on hairy areas. Folliculitis may occur, owing to pitch and paraffin oils.

Avoid changing the dressing often.

Do not apply tar to infected or impetiginized lesions.

Do not apply tar to more than one quarter of the body surface at one time. There is danger of absorption, since coal tars contain from 2 to 4 per cent phenol.

Be on the lookout for evidence of sensitivity after prolonged use.

Keep coal tar and coal-tar pastes in carefully sealed containers to avoid evaporation of volatile ingredients, which constitute a valuable part of their efficiency.

*The coal-tar paste referred to is Daxalan, manufactured by Dome Chemicals, Inc., of New York City; the tar is obtained from the Barrett Company, Edgewater, New Jersey.

Pharmacologic Action

Since coal tar is not a uniform entity, its therapeutic action depends on the aggregate effect of its components. As these vary both qualitatively and quantitatively there must of necessity be minor variations in clinical effects between different samples of tar.

The antiseptic and antipruritic effects depend chiefly on naphthalene and the phenols and cresols. In a dilution of 0.1 per cent, tar exerts a definite astringent action.

The predominant effect of coal tar is keratoplastic, which is dependent on the presence of methylnaphthalene, dinaphthalene, xylenol and naphthol. Sulfur, which is present in a concentration of approximately 0.2 per cent, may contribute slightly to the keratoplastic action.

The reducing action of coal tar is closely related to its keratoplastic effect, and coal tar is exceeded in this respect only by dioxyanthranol, chrysarobin, pyrogallol and juniper tar. It has one distinct advantage over these substances: it can be used on vesicular lesions, which are invariably irritated by the other potent reducing agents.

The ability of coal tar to penetrate the epidermis depends on the presence of distillation products with high boiling points, especially methylnaphthalene. It abstracts oxygen from the skin, thereby inhibiting mitosis and resulting in a numerical and dimensional decrease in the cells of the rete malpighian and corneous layers.

Clinical Use

Infantile eczema. No single topical remedy is so beneficial in this condition as a properly prepared coal-tar paste. Those cases in which the face is covered with a crusted vesicular dermatitis are particularly amenable. The paste is applied in the usual way and a mask of soft light muslin or cotton cloth, fenestrated for the nose, mouth and eyes, is used to cover it. The dressings are changed not oftener than every twenty-four hours.

Occupational dermatitis, dermatitis venenata and *contact dermatitis.* These three dermatoses, which have certain features in common, are invariably benefited, whether they are vesicular or lichenified. With the multiplication of factories and new industries incident to the war, occupational dermatoses assume a new importance. The causative factors may be briefly classified as follows: mechanical irritants (dusts, sand, silicates, carborundum, duralumin, steel filings and so forth); inorganic

chemical irritants (soaps, soda, potash, lime, ammonia, mineral acids and so forth); organic chemical irritants (coal-tar derivatives, dyes, paints, plants and so forth); and mineral oils and greases. One precaution in the treatment of dermatoses due to contact substances is to avoid coal tar if there is much edema or any secondary infection. Cold, wet compresses of Burow's solution or boric acid should be used first to prepare the involved area for the coal-tar paste. Improvement is often dramatic and may be expected within a few days.

Dermatophytosis. Fungus infections of the feet and crotch, when vesicular, and vesicular dermatophytids of the hands respond well to the application of coal tar, although it exerts no direct lethal influence on the infectious agent.

Varicose eczema. Varicose eczema and varicose ulcers are promptly, although often only temporarily, improved by coal tar. In the absence of secondary infection there is no other agent that affords such rapid improvement.

Dermatitis hiemalis. By winter dermatitis is meant a condition characterized by more or less circumscribed, nummular and discoid areas of vesiculation, occurring in the winter, especially on the lower extremities, in individuals with a sluggish peripheral circulation, and accompanied by periodic pruritus. Response to coal-tar applications is good, although at times slower than in other vesicular eruptions. If the paste is applied sparingly and well covered with talcum powder, there is little soiling of the linen. Another method is to cover a thin coating of paste with flexible collodion or latex.

Chronic exudative lichenoid and discoid dermatitis, and *dermatitis exfoliativa.* Pruritus and cutaneous inflammations are greatly improved by coal-tar pastes. Depending on the cause, many patients obtain only temporary symptomatic relief. In all patients with generalized or universal involvement, it is advisable to limit the application to not more than one third of the body surface at one time.

Pityriasis capitis. Although the use of coal tar on the scalp is disagreeable, when the paste is mixed with an equal quantity of a fixed vegetable oil it may be conveniently applied by means of a toothbrush. No dusting powder is used.

Pruritus ani. The response of itching in the anal and perineal regions to coal tar is erratic. When there is an associated dermatitis with fissuring, the effects are better than those in essential pruritus. If improvement is not apparent within a week, treatment should be interrupted, since in this region folliculitis not infrequently complicates tar therapy. In some cases favorable results are prompt and permanent.

Chronic dermatosis. The results obtained in prurigo, lichen simplex chronicus (neurodermatitis) and atopic eczema are frequently as good as those in acute conditions, although they are slower in attainment and often only temporary.

Psoriasis. The improvement following the application of a good coal-tar paste followed by ultraviolet radiation in ambulatory patients is often as good as those following the use of chrysarobin in hospitalized patients. The method used, essentially that suggested by Goeckerman,[5] is as follows:

Remove all scales with green soap and water previous to instituting treatment.

Apply coal-tar paste to the lesions for twenty-four hours and then remove with mineral oil until only a slight brownish stain remains.

Administer mercury-vapor quartz-lamp exposures of just sufficient intensity to avoid a reaction.

Repeat this entire procedure daily, increasing exposures to produce tanning.

Permit the patient to take a bath after each exposure before reapplying the ointment.

Favorable results are frequently apparent within three or four weeks, although, as with other methods of treating psoriasis, they are seldom permanent.

Summary

Differences in various coal tars, and in addition the methods of compounding coal-tar pastes, are responsible for variations in therapeutic response of various skin diseases.

Acquaintance with the physical, chemical and pharmacologic action of a coal-tar paste is essential for the best results.

When properly used, coal tar has a beneficial effect in a large group of acute and chronic inflammatory dermatoses.

The most satisfactory results follow the use of a paste of standard manufacture.

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CORNEAL TRANSPLANTATION

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THE subject of corneal transplantation or keratoplasty has become fairly familiar to ophthalmologists in recent years, and the operation itself is being done with increasing frequency. It should be even more important in the near future in military medicine, since a large number of eyes will undoubtedly be blinded from corneal scars due to traumatic injuries with infection or to burns. Since this operation is now a well-established and fairly successful medical procedure, it appears to be of interest to the profession at large.

Transplants are classified in two ways; by surface area and by depth. According to area, they are total if the entire width of the cornea is used, and circumscribed, or partial, if only a window is taken from the cornea. According to depth, they are lamellar when only the top layers or lamellas are replaced, and penetrating when the full thickness of the cornea is transplanted. Thus one recognizes four types of keratoplasty, total lamellar, circumscribed lamellar, total penetrating and circumscribed penetrating. Only the last one has a practical significance. Lamellar keratoplasty is a conservative procedure; but since a slight layer of scar tissue forms between the new and the old lamellas, it cannot give as good a visual result as a full-thickness, clear corneal graft. Total penetrating keratoplasty, involving replacement of the entire cornea, with or without some of the adjacent conjunctiva or sclera, has been tried many times, but the results have always been poor and have frequently necessitated subsequent enucleation.[1] Hence, the most popular operation at present is a circumscribed penetrating keratoplasty. In this procedure, windows 4 to 6 mm. wide are cut through the full thickness of the opaque cornea and replaced with pieces of clear corneas from enucleated eyes.

As with skin grafts, one also speaks of autotransplants (in the same individual), homotransplants (in the same species) and heterotransplants (between species, as from cat to man). The first and second appear to work equally satisfactorily, but heterotransplants, despite some temporary improvement, have never given a successful result in either man or animals.

Numerous methods of transplantation on both animals and human beings have been tried by many surgeons during the past hundred years, but only during the last two decades has clinical improvement ceased to be regarded as a minor miracle. During the 1920's, Elschnig,[2] in Prague, and Filatow,[3] in Odessa, did a large number of round transplants with trephines, with a few good results. In 1930, Thomas,[4] in England, made an important contribution by beveling the edges of his trephine grafts. He[5] has had many excellent results since that time. In 1932, Castroviejo,[6] in New York, published his first animal experiments, and since then he[7] has made a greater number of important contributions to this subject, both clinically and experimentally, than any other ophthalmic surgeon.

The object of corneal transplantation is to restore sight to eyes blinded by opacities in the corneas. Unfortunately, not all such cases are suitable for operation. Favorable cases are those in which the eye is normal except for the cornea, the leukoma or scar is not dense or vascular; and there are areas of clear or slightly scarred cornea surrounding the graft to furnish it nutrition. Especially unfavorable cases are those with dense scarring of the entire cornea or with a vascularized pannus, such as that which comes from old trachoma. The eye can sometimes be rendered suitable for operation in the latter type by removing the pannus and using diathermy to seal the vessels at the corneal margin. Eyes with an old interstitial keratitis or conical cornea are unusually satisfactory cases for transplantation.

Another limiting factor in this field of surgery is the availability of donor eyes. Any enucleated eye with a clear cornea can be used. Such corneas are found in cases of intraocular tumor or blind and painful glaucomatous eyes where the cornea is edematous but has not yet degenerated. Eyes from newborn babies are also often used. Fresh material is best, but fair results are reported in eyes refrigerated for twenty-four hours.

Methods of operation are numerous. The most successful one is the graft developed by Castroviejo.[8] A square is cut two thirds of the way through the cornea with a double parallel-bladed knife. An oblique penetrating incision is made in the anterior chamber with a small triangular knife, or keratome, at the upper margin of this square. The square is then excised with special scissors, leaving the edges slightly beveled. The transplant is cut from the donor eye with the same knife and carefully slid into place from a flat spatula. The beveled edge on the host keeps this graft from getting lost in the anterior chamber, and several cleverly designed cross-stitches help prevent external dislocation.

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The circular graft of Thomas[5] is also fairly satisfactory. A trephine hole is made two thirds of the way through the cornea, then continued at an angle so that an oblique penetration is made on one side. The cutting is completed with scissors, leaving a slight bevel. The graft is held in place with one vertical and one horizontal cross-stitch. Castroviejo[7] has also perfected a modification of this method. Although I have never tried the Thomas stitch, I believe that the Castroviejo suturing is considerably more efficient.

Recently Wiener and Alvis[9] introduced a method of cutting a slightly beveled graft with a corneal punch inserted through an incision near the corneal margin. This is by far the easiest procedure to carry out and the graft fits perfectly, but so few cases have been done by this method that its exact value is still unsettled. The peripheral incision probably does not hinder healing, but it leads to formation of anterior synechias or adhesions if a previous iridectomy has not been done. The synechias, of course, increase the danger of glaucoma. With this method, furthermore, unless the sutures are placed quite far out on the cornea it is easy to cut one when the bite is made; and if cut, a suture cannot safely be replaced.

Following operation, the patient is kept quiet in bed for ten to twelve days, and both eyes are covered for eighteen to twenty days. The pupil is kept dilated with atropine. The transient edema of the graft passes off during the first two or three weeks, and at the end of one month all but the periphery of the graft is clear and union is quite firm. Microscopic sections show conclusively that a successful graft retains its cellular identity and is not replaced by new tissue.

In unfavorable cases the graft usually takes, but soon becomes cloudy because of vascularization, proliferation of connective tissue on the back of the cornea or low-grade degenerative changes in the deep corneal layers, with loss of the normal parallel fiber arrangement there.

My own practical experience with keratoplasty has been limited to the last four years. The actual operation on human beings was approached in a rather guarded manner, with the result that up to the end of 1941 I had completed only 10 cases, one patient at that time having had a clear corneal graft for three and a half years. Because of this early caution, all these cases were classed as unfavorable in that they had dense or complete corneal scarring, vascularization or another ocular defect, such as former glaucoma or cataracts, nystagmus, chorioretinitis or extremely advanced and still active corneal dystrophy. The operation was also limited to eyes that had less than 5/200 visual acuity and that, in addition, had a markedly defective companion eye.

The results were surprisingly good, however, since all grafts took, and all cases were improved (Fig. 1). The poorest result was in a case of vascularized and thickened complete leukoma of the cornea, which a keratoplastic surgeon in another city had refused to treat. The patient's vision six months after operation was limited to hand movements, but his original vision had been reduced to poor light projection with the ordinary flashlight, and he regarded himself as seeing considerably better. A patient treated recently also had a cataract, but it was thought best to do the transplantation first. As he has not yet had the cataract extraction, his vision is still poor; the graft, however, is crystal clear, so that the visual result will probably be good. The other cases have shown marked improvement, and several of the patients can read ordinary book print, including 2 patients with nystagmus and 2 with considerable myopia. Despite this ability to read, however, no patient has better than 20/70 vision.

These operations were done with the square graft of Castroviejo. More recently, however, I did my first punch-type transplantation. The graft took and was clear, but it had apparently slipped down slightly, leaving a tiny gap superiorly. This was the first time I had had any leakage from a wound. At the end of three weeks a conjunctival flap was put across the defect and at present it is still in situ. As the graft was transparent at the time of the flap, a satisfactory outcome is hoped for.

* * *

It is obvious from the work done in this field that corneal transplantation is a practical and not too dangerous operation. It seems best, however, to follow the custom already adopted elsewhere of operating on suitable cases with vision of 15/200 or less rather than selecting only the few extremely bad cases. As these corneas are more favorable to work on, future results may well include some normal or near-normal visual acuities.

9 Central Street

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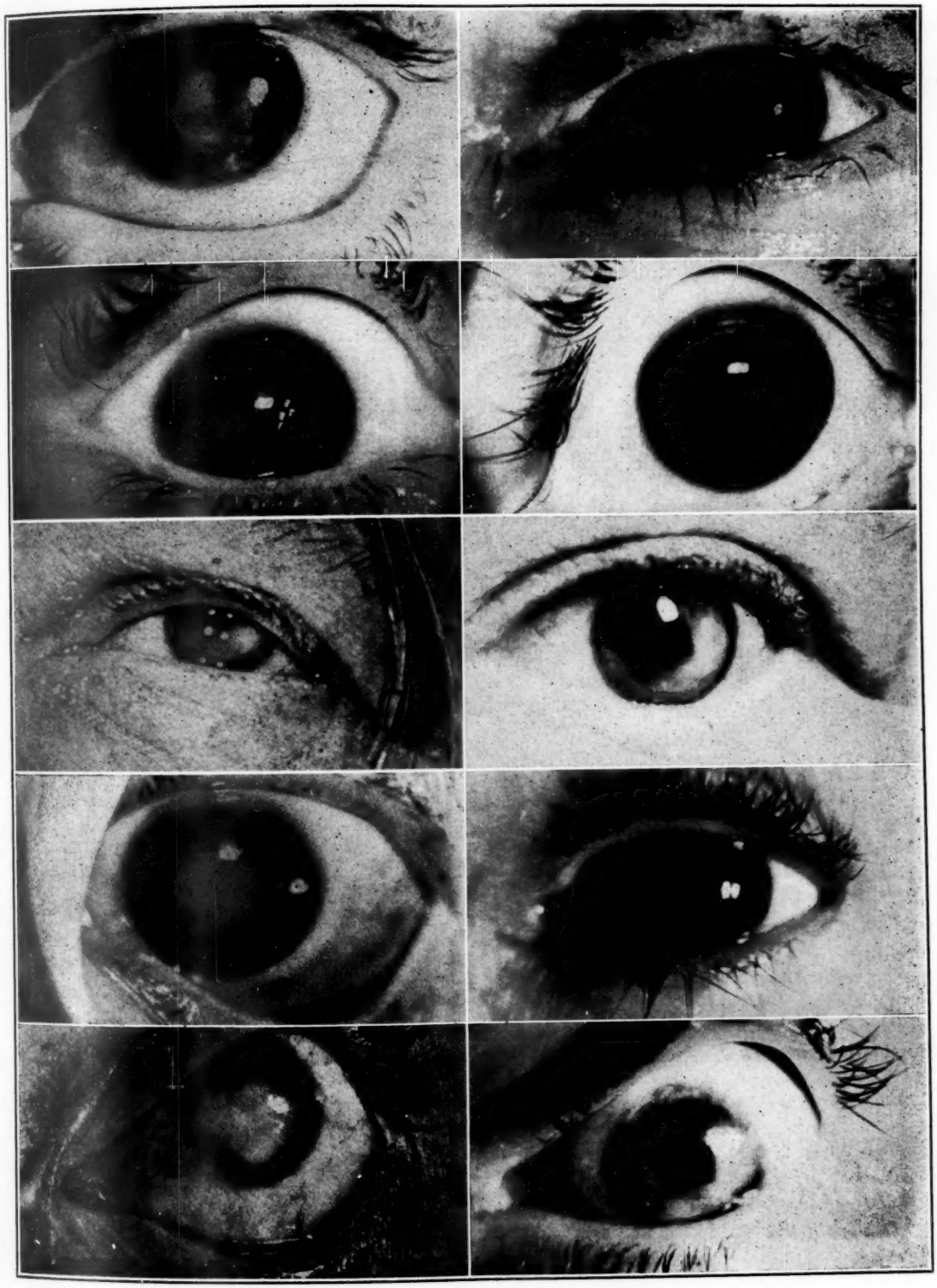

FIGURE 1.

Cases of Corneal Transplant Showing the Eyes of 5 Patients before and after Keratoplasty.

CLINICAL NOTE

PELLET IMPLANTATION*

The Subcutaneous Implantation of Crystalline Pellets of Hormone

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SINCE the investigations of Deanesly and Parkes[1, 2] on the subcutaneous implantation of crystals or compressed tablets (pellets) of androgens and estrogens, many papers have appeared in the literature describing this method of administering hormones of various types. These authors have shown that pellet implants are especially desirable when a prolonged steady effect is required, thus obviating the necessity of frequent injections of hormone over long periods of time. Using pellets of desoxycorticosterone acetate subcutaneously in adrenalectomized dogs and later in patients with Addison's disease, Thorn and his associates[3, 4] reported excellent results and emphasized the advantages of administering hormone in pellet form. As a result of this advance in the treatment of certain hormonal deficiencies, a number of reports[3, 5, 6] have appeared in the literature describing ways and means of facilitating the operative implantation of pellets of crystalline hormone subcutaneously.

This paper describes another operative technic that has been found successful in the subcutaneous implantation of pellets of desoxycorticosterone acetate in patients with adrenal insufficiency. It is believed that this procedure may be successfully employed to implant crystalline pellets of other hormones as well.

Implantation should be performed in the operating room under the usual aseptic precautions. The necessary instruments are simple and are found in most hospitals. The essential material is as follows: trocar and cannula (Fig. 1); glass rod; hypodermic syringe and needles; 1 per cent solution of novocain; scalpel; forceps; and suture material.

Experience has shown that the infrascapular region is best suited for pellet implantation (Fig. 2*A*). After a routine skin preparation, an intradermal wheal is made with 1 per cent novocain. With a long needle the subcutaneous tissues are infiltrated within an area of several centimeters. An incision about 1 cm. in length is made at the anesthetized site. A trocar with attached cannula

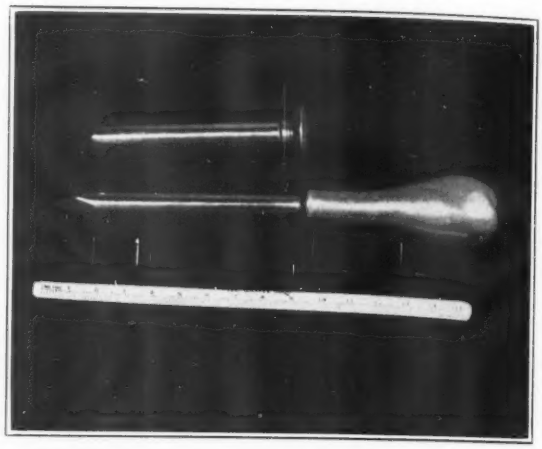

Figure 1. *Photograph of Trocar and Cannula.*

is easily introduced through the skin opening and gently forced into the subcutaneous tissue (Fig. 2*B*). The trocar is withdrawn, leaving the cannula in place (Fig. 2*C*). With forceps a pellet is

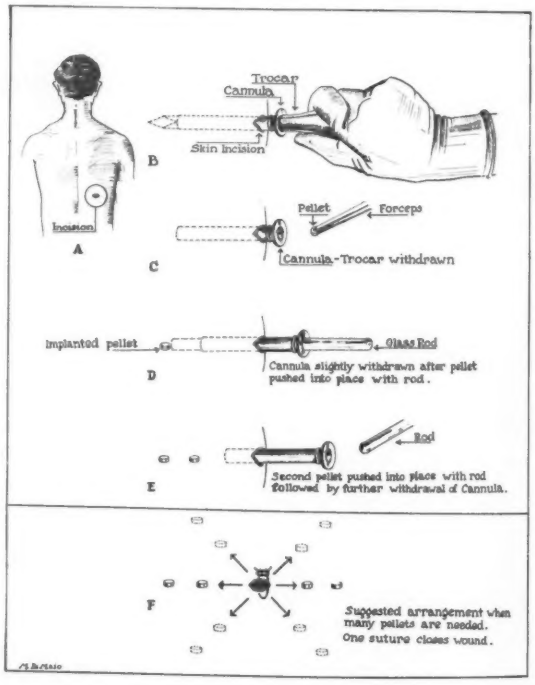

Figure 2.

inserted into the lumen of the cannula and pushed into place with the aid of a glass rod (Fig. 2*D*). With the pellet held gently in place by the rod, the cannula is carefully withdrawn for about 1.5

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cm.* The glass rod is then completely removed and a second pellet is directed into place in a similar manner. The procedure may be repeated if a third pellet is to be implanted on the same side, but the operator should make certain that the cannula is withdrawn a short distance when each pellet is in place (Fig. 2*E*).

Following the implantation of one, two or more pellets on one side of the incision, the cannula is completely withdrawn. If more pellets are to be implanted, the trocar with cannula is inserted through the same skin opening but in the opposite direction, and the procedure is repeated. Should the patient's condition require inserting a large number of pellets, this is readily done by directing the trocar in other directions, always using the original incision (Fig. 2*F*). A single suture is all that is necessary to close the wound.

This procedure has many advantages. It has proved to be simple, short and effective. Trauma to the tissues is held at a minimum. Bleeding is negligible and hemostasis is not necessary. The gentle handling of pellets is assured; this is important, since crushing of one or more pellets may be harmful. Furthermore, since pellets are placed several centimeters from the incision they are not easily extruded, as has occasionally been found to be true with other procedures. The clumping of pellets does not occur. Virtually any desired number of pellets may be implanted without difficulty. Likewise, the arrangement facilitates the location and removal of one or more pellets through a small incision should the occasion demand it.

*The outside of the cannula may be graduated in centimeters, but this is really unnecessary.

Summary

A simple, short operative technic has been described for the implantation of pellets of hormone under the skin with the aid of a trocar and cannula.

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MEDICAL PROGRESS

THE USE OF DRUGS IN THE TREATMENT OF ASTHMA

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MANY articles have been written on the use of drugs in the treatment of asthma in the last few years, but there still seem to be difficulties and misunderstandings in various directions. It is consequently worth while to review the recent knowledge and to add one or two personal observations.

EPINEPHRINE (ADRENALIN)

When a patient is younger than thirty-five and the onset of asthma was before or about the age of twenty, the chances are good that the cause is not some pathologic lesion (intrinsic factor), but that it depends on a hypersensitiveness to a food, dust or drug in the environment (extrinsic factor). In such a case it is quite proper to inject a small dose of epinephrine subcutaneously. If the attack is relieved, further doses can be given three, four or perhaps six times every twenty-four hours while the patient is at home. If, however, the asthma is severe and the doses of epinephrine have only a slight and transient effect, the patient should be removed to a hospital. The details of further treatment are relatively unimportant. Such patients will almost surely do well in the hospital, simply because they have escaped from the causative substance at home. The doctor should not be overanxious to relieve the wheeze during the first few hours after admission. If the cause is a dust and the patient has escaped, the asthma will clear by itself. Also, the fatigue and anxiety which go with asthma will improve with the nursing care and the reassurance that are so important a part of the hospital management.

Epinephrine is the blood-pressure-raising constituent of the adrenal gland isolated by Abel[1] in

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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1897, and renamed "Adrenalin" by Takamine[2] a few years later. It is a sympathicomimetic substance the function of which is to stimulate the sympathetic nerves to make them overcome the action of the vagus nerves, which produce the asthma. In most cases the stimulation is effective, but if the drug is used repeatedly or given in too large doses, after a time the sympathetic nerves become overstimulated and the nerve-muscle cannot respond. The epinephrine is then said to have lost its effect.

The symptom asthma may be produced by a spasm of the smooth muscles in the bronchial wall, by a swelling of the mucous membrane or by an overactivity of the mucous glands. One or another of these results in a narrowing of the bronchial lumen and so in a wheeze. Whether the effect depends on a central and therefore a direct nerve stimulation or on the local action of some chemical effector substance like histamine or acetylcholine, which acts directly on the effector organ — the mucosa, the muscle or the glands — is still debatable, but the fact is that the result is a diffuse process which causes the signs of asthma to be fairly evenly distributed throughout the lung. In typical extrinsic asthma the signs are not limited to any one area.

Epinephrine is sometimes called on to stop the cough from bronchitis, with its mucus in the lumens of the bronchi, the dyspnea of heart disease, with its engorgement of pulmonary blood vessels, or the dyspnea of organic emphysema, with its dilatation and coalescence of terminal alveoli and its large spaces filled with air. But the drug cannot relieve these conditions: it is effective only when the symptoms are due to excessive vagal stimulation.

The dosage of epinephrine is important. When the correct dose is given to the right patient, the asthma is relieved, no new symptoms develop, and no harm results. When, however, too much epinephrine is used, the asthma itself may improve but the patient feels "queer." He turns pale and sweats slightly, the hands become cold, and the pulse becomes rapid and the heart pounds. There may be headache, and with all this a sense of weakness and collapse. In some ways the picture resembles that of surgical shock, but the blood pressure is usually higher, not lower, than normal. These side effects depend obviously on the stimulation of other parts of the sympathetic system. Thus, the heart is stimulated and the blood pressure rises; if continued, the effect may result in auricular fibrillation. As an example of severe reactions, a man of forty-two was seen at home on the third day of a severe asthmatic attack. His wife had given him epinephrine every 2 hours as instructed, but the drug ceased to be effective. Unfortunately, the pallor, sweating and rapid pulse observed were not recognized as due to an excess of the drug, but were attributed to fatigue and loss of sleep. Still more epinephrine was injected. Within a few minutes the shock increased. The breathing became shallow, and the patient became almost unconscious. He was given ¼ gr. of morphine and hurried to the hospital. An intravenous infusion of 5 per cent glucose in physiologic saline solution was started and the patient rallied, his color and pulse returning to normal.

Such reactions from the injection of watery solutions of epinephrine are, however, infrequent. Keeney[3] reports the case of a man of thirty-three who was given 0.5 cc. of a 1:1000 dilution by hypodermic injection. Violent headache with coma developed in a few seconds. The next day the patient had a right hemiplegia. He recovered slowly. The drug may have been injected intravenously by accident; many lesser reactions have come from that circumstance.

Three practical points are worthy of emphasis. In the first place, epinephrine is effective only when the patient's symptoms depend on spasm of the bronchial muscles or swelling of the bronchial mucosa. Secondly a small dose, that is, 0.25 cc., is usually quite as effective as a larger one. Patients vary in this regard, however, and it may happen that a given patient requires a large quantity. One should begin with a small dose and increase it gradually until the desired effect is obtained, after which it may be possible to reduce it. If the first dose is ineffective, a second may be injected in about fifteen minutes. Such pairs of doses, however, should not be given oftener than two hours apart. The intravenous injection of 1 liter of physiologic saline solution containing 1 cc. of a 1:1000 dilution of epinephrine is a useful procedure in cases of critical severity. And, finally, too much epinephrine does much more harm than good. If the patient has had repeated injections with no effect, the administration of further quantities may lead to serious difficulties.

High blood pressure is not a contraindication to the drug provided that bronchial spasm is present at the same time. When this bronchial spasm is relieved, the burden on the heart is lightened and the blood pressure goes down.

The effect of epinephrine appears within fifteen minutes. It may persist for many hours, but in most cases it lasts for not more than two to four hours. Efforts to prolong the effect have been made.

The administration of epinephrine in oil was suggested in 1938 by Keeney.[4] The powdered base is suspended (not dissolved) in sterile peanut oil—

2 mg. per cubic centimeter or a 1:500 suspension. In Keeney's first experiment olive oil was used, but later he and his associates[5] found that peanut oil was less irritating, since it contains less fatty acid. The usual dose is a whole ampule, or 1 cc. For some patients, the method is satisfactory, and the asthma is relieved for a longer period than it is by the ordinary watery solution. The fact that the speed with which relief of symptoms comes is about the same with oily as with watery epinephrine indicates that absorption at least begins promptly.

Reactions to epinephrine in oil, however, are not infrequent. In a recent paper, Keeney[6] has reviewed them. Local reactions, consisting of redness, swelling and pain at the site of injection, depend on the presence of an irritating fatty acid in the oil or, more rarely, on an allergic response to the oil itself. More important are the systemic reactions. Symptoms of overdosage — pallor, palpitation and nervousness — not infrequently follow doses of oily epinephrine. Keeney reports 4 cases in which the symptoms were alarming. He points out that the large needle required for the oily mixture leads to rapid injection, and that the danger of placing the material in a blood vessel is greater than when the injection is given more slowly and through a smaller needle. Since in oil the epinephrine is present in a strength of 1:500 instead of 1:1000, one should be particularly careful not to inject the dose into a vein. Whether trouble comes because the epinephrine is a suspension of dry particles rather than a true solution Keeney considers doubtful. Dorwart[7] reports the case of a woman of twenty-two with asthma who was given 0.3 cc. of 1:1000 aqueous epinephrine and at the same time 1.0 cc. of oily epinephrine. Within a few minutes there occurred shaking, pallor, twitching and cyanosis, with a pulse rate of 160, and the patient's condition became desperate. It was relieved temporarily by tourniquets, but she was not out of danger for five hours. More recently Maietta[8] has reported that of 14 patients treated with epinephrine in oil, 2 had severe reactions. A man of thirty-seven with severe asthma was given 0.4 cc. of watery epinephrine and ten minutes later 1.0 cc. of epinephrine in oil. The effect was severe for one and a half hours. An obese woman of thirty-eight suffering from asthma of moderate severity was given only 0.4 cc. of epinephrine in oil. Within an hour came blanching at the site, followed by redness and swelling, which spread over the shoulder, arm and forearm. The local lesion lasted for six days.

Gelatin provides another medium for the administration of epinephrine, as Spain, Strauss and Fuchs[9] have described. It is prepared by adding one part of a 1:100 aqueous solution of the drug to four parts of an aqueous solution containing glycerin, sodium chloride, sodium bisulfite and chlorbutanol. At room temperature this solution gels, so that the ampule must be warmed before injection. The usual dose of 1 cc. contains 2.0 mg. of epinephrine. It can be given subcutaneously. In 50 cases the results were good and no untoward reactions were observed. Miller et al.[10] have used epinephrine in gelatin in over 200 cases, and find it useful.

Epinephrine given as a spray to be inhaled directly into the bronchi was used first by Graeser and Rowe[11] in 1935. A relatively strong (1:100) dilution was employed — generally in a special fine nebulizer — and a large number of asthmatic patients were treated. If the bronchospasm was not severe, this method was found to be effective. Galgiani et al.[12] calculate that each squeeze of the bulb discharges only 0.008 mg. of epinephrine. Even so, they found that when rabbits and cats were given ten squeezes of this solution each day, after four months there was a loss of cilia and a desquamation of the tracheal and bronchial epithelium in some of the animals. Another slight risk is that the bottle of the former 1:100 epinephrine may be mistaken for that of the ordinary 1:1000 solution, and that a dose of the former may be injected subcutaneously. In one such case reported by Gormsen[13] the patient died in a few minutes from a dose of 0.6 cc. (60 mg. of epinephrine) of the solution.

New products designed as substitutes for epinephrine have recently been reviewed by the Council on Pharmacy and Chemistry.[14] Vaponefrin contains racemic epinephrine having the levorotatory and dextrorotatory isomers in equal parts (epinephrine *U.S.P.* is purely levorotatory). The dextrorotatory isomer is the much less active of the two, but analysis has shown that whereas the material as prepared contains 23 mg. of substance per cubic centimeter, it has a physiologic activity equivalent to that of 1:40 dilution of epinephrine. Vaponefrin is sold only to physicians, but products entirely similar are sold to the public under such trade names as Asthmanefrin, Neosol (also called Solution A or Inhalant A) and Nepheron (also called Solution N or Inhalant N). Each of these is active and effective but expensive, as Barach and his assistants[15] point out.

Epinephrine consists chemically of a benzol ring with two hydroxyl (OH) groups and a chain made up of two carbon and one nitrogen atoms. The hydroloxyl groups on the ring make the compound unstable and give it optical activity. Further details concerning epinephrine appear in a comprehensive paper by Cori and Welch.[16]

Ephedrine

Ephedrine is closely related to epinephrine. It has no hydroxyl (OH) group in the benzene ring so that it is stabile and is not optically active. The drug is useful in asthma; it is absorbed by mouth and controls mild bronchospasm. Its action is slow, and the dose, 20 to 40 mg. (⅜ to ¾ gr.), should be taken after supper if the effect is to be obtained at bedtime. Too much ephedrine may cause palpitation and tachycardia. The commonest difficulty, however, is that the drug causes sleeplessness, and on this account ephedrine has been mixed in various proportions with barbiturates and dispensed in capsules of many colors by different drug companies. Ephedrine is worth a try, perhaps, but if it does not control the symptoms, the patient should be given epinephrine, in place of forcing the dose of ephedrine to high levels. An interesting innovation is that of Brown,[17] who coated ephedrine with a wax so as to delay its absorption for about three hours. By taking this tablet at bedtime, together with a dose of regular ephedrine, the patient receives a new dose of ephedrine automatically at about the time when the effect of the regular ephedrine is wearing off.

Aminophylline

Aminophylline is a combination of theophylline with ethylene diamine. It was first used in 1937 by Herrmann and Aynesworth[18] as a treatment for severe asthma. In the same year appeared a paper by Greene, Paul and Feller[19] in which the drug was advised as a treatment for cardiac failure. These authors found that after the drug was given the breathing improved and the pressures in the vein and in the spinal fluid rose.

Theophylline is a xanthine derivative related to caffeine and to theobromine. All these drugs have a diuretic action, presumably because they improve the transport of fluid through the kidney capillaries. The addition of ethylene diamine to theophylline renders the mixture much more soluble, so that the combination called aminophylline is much more effective than is theophylline by itself.

In asthma the effect is good. Young and Gilbert[20] believe that aminophylline has a protective action against the bronchial constrictor effect of histamine. In guinea pigs, histamine shock and anaphylactic shock are both inhibited if the test dose is preceded immediately by an injection of aminophylline. So far, the mechanism that results in the relief of asthma by aminophylline is not clear.

Aminophylline must be given intravenously. If given subcutaneously it is much less effective, and furthermore it is irritating to the tissues. The dose for intravenous injection to the average patient is 200 mg. (3⅜ gr.), which is dissolved in 10 cc. of water and comes prepared in ampules. A larger quantity, up to 400 mg., has been used, but is no more effective than the smaller dose.

Another preparation consists of 400 mg. dissolved in only 2 cc. of fluid. Supposedly this preparation is for intramuscular use. Occasionally, however, this concentrated material is given by vein; in such cases the patient has a sense of flushing and warmth, with palpitation and weakness, that may be quite troublesome. So far, severe and dangerous reactions following the use of aminophylline have not been described. Lamson and Bacon[21] have used it freely, and even though their clinical description is long and complete, they say little about untoward effects. Incidentally, they find that the symptoms of hay fever and urticaria are improved by aminophylline quite as much as are the symptoms of asthma.

Aminophylline is prescribed in doses by mouth. The literature contains little about this topic, perhaps because the effect is hard to evaluate; certainly it is rarely striking. In the Allergy Clinic of the Massachusetts General Hospital, aminophylline is given in pills containing 0.2 gm. (3 gr.), to be taken three or four times a day. Several commercial preparations contain 2 gr. of theophylline in combination with ⅜ gr. of ephedrine and ⅛ gr. of phenobarbital. One in common use has 2 gr. of aminophylline in a similar mixture. Many patients declare that the ingestion of one, two or three of these tablets or capsules each day seems to protect them from their attacks. No doubt more are consumed than are really necessary.

Water, Salt and Sugar

Almost all patients with severe symptoms that cannot be easily controlled should be given an intravenous injection of normal salt solution, usually containing 5 per cent glucose; a relatively large amount (1500 cc. or more) is allowed to run in with fair speed. In most cases the effect of this simple procedure is prompt and satisfactory. Patients with severe asthma cannot eat or drink. They have a tired, pinched expression, the tongue is parched, and they are dehydrated. To give such a person 1500 cc. of water containing 12 gm. of sodium chloride and 75 gm. of glucose helps very considerably. Sometimes improvement from this treatment begins promptly and develops dramatically when only 300 or 400 cc. has been run in.

The mechanism of this improvement is not at all clear. So far no studies of blood constituents or of the distribution of electrolytes have been made in asthma, and the field needs cultivation. Whether the addition of sugar accomplishes anything more

than providing a little food seems doubtful. In 1937 Wagner and Rackemann,[22] among others, studied the glucose tolerance of patients with severe asthma, some of whom were in status asthmaticus, but found that the curve was like that for normal nonasthmatic subjects. The sugar metabolism in asthma appeared to be normal. Whether the injection of physiologic salt solution by itself without the addition of glucose is equally effective can be determined easily, but curiously it has not been tried in any series of cases.

Hypertonic glucose solutions have been advocated. In 1934 Lepak[23] at the Mayo Clinic treated 4 cases of severe asthma by injecting intravenously 100 cc. of 50 per cent glucose on each of two or three days and claimed good results. In 1938 Stoesser and Cook[24] gave similar treatment but in smaller doses to 3 children, and found that when the asthma was due to food allergy the attack was relieved, but when it was due to dusts the effect was not so good. Incidentally, children without associated pharyngitis and bronchitis responded better than did children with these secondary infections. In the same year Keeney[25] treated 6 patients with one or more intravenous injections of 100 cc. of 50 per cent sucrose (not glucose) to which had been added 0.5 cc. of a 1:1000 solution of adrenalin. In all, twelve injections were given, and with only two exceptions there was immediate relief from asthma, which lasted for at least two and a half hours. Stoesser and Cook[24] also used sucrose, but not with such good results.

Other Drugs

Potassium salts. Potassium iodide has been described as the "sheet anchor" in the treatment of asthma. Most authors consider that its effect depends on its excretion into the bronchial tubes, where it irritates the mucous membrane and the mucous glands and so increases bronchial secretion. In this mechanism more stress has been laid on the iodine than on the potassium radical. Now, however, there is evidence that the potassium radical may be important. In 1938, Rusk and Kenamore[26] made the interesting observation that the injection of epinephrine causes an increase in the potassium concentration of the blood serum, and also that the intravenous injection of potassium salts relieves the symptoms of urticaria. Potassium lowers the irritability of the skin, making it less responsive to local irritation. Putting these facts together, the authors devised a "potassium regime." They made the diet low in sodium and high in potassium for the treatment of urticaria and of allergy. In the next year Rusk and his co-workers[27] found that potassium is stored in the tissue cells of the body, and that in allergy this store is depleted. Keys[28] found that after the giving of epinephrine the plasma potassium falls but returns to normal in about twenty minutes. Evidently epinephrine produces a change in the distribution of the potassium between cells and plasma. Since 1938 the use of potassium chloride has been discussed frequently, but unfortunately with no unanimity of opinion. Cohen[29] used the diet and the potassium chloride that Rusk and Kenamore advised, but saw no change in 8 patients. Bloom,[30] however, declared that it produced striking benefit in 29 cases of hay fever. Rusk himself gave potassium salts to 30 patients with hay fever, but with good effect in only 3 of them. Fürstenberg and Gay[31] gave potassium chloride to 85 per cent of the patients in the clinic at Johns Hopkins Hospital, varying the doses and technic considerably, but the results were uniformly poor. Harsh and Donovan[32] gave potassium chloride up to 18 gm. per day but were not at all satisfied that it did any good, for, as they point out, other factors could explain the small variations in the symptoms described. Obviously, there is much to learn about the physiology of allergy, especially of the asthmatic attack, and as said before, one can hope that accurate and complete data on the subject will be forthcoming.

Insulin. Bruhl[33] found that the intravenous injection of 10 units of insulin — he called it the "insulin thrust" — was useful in allergic skin disease, especially urticaria, and he tried the method in asthma, hay fever and mucous colitis. He is convinced that it is possible to influence allergic processes with insulin therapy. Insulin burns up sugar and lowers the blood-sugar level, and its effect is quite opposite to that of hypertonic glucose solutions. The results claimed for the "insulin thrust" make the problem even more confusing.

Sodium thiosulfate. The use of this drug is advocated by Klein[34] on the basis of some alteration in the body colloids. He has used it both by mouth and by vein in allergic epilepsy, in migraine and in urticaria, and declares that his results have been unusually excellent.

Amino acids. Tryptophan and histidine have been used by Lenormand,[35] who believes that they stimulate a hypersecretion of mucus, which in turn protects the hypersensitive membrane.

General anesthesia. It has been frequently observed that general anesthesia stops asthma temporarily. Perhaps this explains some of the beneficial results claimed for various operations that have been advised in the treatment of asthma. Anesthesia without operation has been tried; although this may provide temporary relief, the results are not so good as they are when some operation is combined with it. The prolonged

effect of the latter may depend on tissue injury, with the subsequent absorption of tissue-degradation products.

Ether. Ether in oil by rectum has been used occasionally. The results are satisfactory, and the mixture is not nearly so irritating to the bowel wall as one might expect. The dose is 30 cc. of ether and 30 cc. of olive oil, shaken well together and injected slowly into the rectum once, twice or even three times a day, if necessary.

Dilantin Sodium. This drug has been used as an anticonvulsant in epilepsy. Quite recently Shulman[36] gave Dilantin to 7 children with asthma in doses of 10 to 20 mg. (1½ to 3 gr.) per day and found the results good. The relief was maintained by continuing the drug in small doses once or twice a day. One must observe, however, that in children especially severe attacks of asthma are often followed by a remission, particularly if the patient is in a hospital.

Niacin (nicotinic acid). Maisel and Somkin[37] gave 100 mg. of niacin by intravenous injection to 20 patients with severe asthma. Sixteen of them were relieved within a few minutes. To 9 other patients doses of 200 mg. were given each day by mouth, and 5 were benefited. The use of this drug deserves further study.

Sulfonamides. The sulfonamide drugs have been used in asthma (Unger[38]), and it is inevitable that many reports about them will be published. So far, however, the results are not encouraging, and the reason seems clear. Asthma does not depend on an acute infectious process. If bacteria are concerned, it is only because they have produced some chronic infection in the bronchi or nasal sinuses, and it is evident that the chronic process is always associated with pus. Since pus antagonizes the bacteriostatic action of the sulfonamides, in such cases the drug has little effect on the bacteria. To use sulfonamide drugs in asthma is like using epinephrine for heart disease: one is asking the drug to do something that it cannot do.

Histamine. The relation of histamine to allergy and asthma is always interesting. Dzsinich[39] first called attention to the treatment of allergic persons by giving them small doses of histamine. Little attention was paid to his work until Farmer and his co-workers[40] became interested in the clinical use of histamine. Histamine and acetylcholine are two substances that are normally present in the body tissues and are released by injuries to these tissues. Histamine comes from muscle and connective tissue, whereas acetylcholine comes from nerves. Together they are referred to as "cholinergic" substances. It is a temptation to consider them as the common denominators that give rise to the symptoms of hay fever and asthma, a relatively uniform picture that is activated by a wide variety of exciting causes. To consider that asthma depends on an over-reaction to histamine or perhaps to an excess of histamine production is tempting, and so it is natural to consider the administration of histamine in an attempt to modify the natural reaction to it. So far the method is still experimental, and is not without danger, since histamine is a potent drug and doses above a certain limit are likely to cause reactions of considerable severity. Particularly in asthma, the treatment if given unwisely can easily precipitate an attack of great severity. The treatment gives some promise, but the details need careful study, and for the moment they had better be left to those who are thoroughly familiar with the drug and with the reactions that it produces.

Ether in oil from an ampule containing 1 cc. of ether and 1 cc. of peanut oil to be injected intramuscularly has been advocated by Maietta.[41] Four patients with acute asthma were relieved by only one dose, and 2 others required two doses. In a group of patients who had had asthma for thirty or forty years, ether in oil given once or twice a week seemed to reduce the severity of the disease and to make other treatment more effective. And, finally, 2 patients with status asthmaticus were given ether in oil at intervals of 4 to 6 hours, with benefit. According to this first report the drug is useful.

Drug Allergy

The literature on drug allergy is extensive, and part of it was reviewed in these columns in 1941.[42] The symptoms are varied; they may be severe, and they appear when least expected. Three drugs are pertinent to the present discussion. *Aspirin* may be effective in asthma, but it should never be given without inquiring carefully whether the patient has ever had trouble from aspirin or other salicylates. Those patients sensitive to aspirin constitute a serious and difficult group. *Barbiturates* of all kinds are in a similar category. A hypersensitiveness to them may be present, and a pill taken to induce sleep — or, more important, a commercial preparation that contains phenobarbital — may not only fail to induce sleep in the patient, but may lead to a bad night for the doctor as well. The situation can become alarming. *Morphine* is important. I believe that it should never be used in asthma, although, in the case cited earlier I did give it when too much epinephrine had created a critical situation. Morphine is a cholinergic drug: it can actually cause bronchospasm. Furthermore, in severe asthma when the patient is gasping for breath, depression of the respiratory center may be the last straw. As the old darky said:

"Sam had the asthma powerful bad, but dat doctor is a great man. After he come, Sam he died jess so quiet."

* * *

From all this, it is quite clear that in asthma, as in other diseases, success in the use of drugs depends on the happy correlation of the physiologic mechanism of symptoms with the pharmacologic effects of the drug selected. To expect drugs to have an effect on a process that they cannot influence leads to discouragement, and sometimes to disaster.

263 Beacon Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29121

PRESENTATION OF CASE

A seventy-five-year-old Massachusetts-born farmer entered the hospital with the complaint of difficulty in swallowing of about ten years' duration.

Some fifteen years before entry he began to have "dyspepsia." This was characterized by slight pain in the "pit of his stomach" and much gas but no nausea or vomiting, and had no relation to the intake of food. An x-ray examination was alleged to have shown a "fallen stomach," and for some years the patient slept with his feet higher than his head, with apparent relief. About five years later he first noticed slight difficulty in swallowing large objects. Two years before entry he had great difficulty one day in swallowing a raisin, and only after an hour and the eating of considerable soft pudding did it finally slip along. Since that time solid food particles frequently stuck at a level that seemed to be slightly below the larynx. Ordinarily he was able to milk them down by rubbing his neck from above downward. No progression in the degree of obstruction was noted, although he ate only soft foods, until two days before entry, when he was completely unable to swallow a mouthful of custard pie. He had eaten nothing since then but had been able to swallow saliva and water. Throughout the ten-year period he had had no pain, nausea, regurgitation or vomiting. He had not lost weight and there had been no cough, hoarseness or change in character of the voice.

The family and marital histories were noncontributory. The patient had habitual constipation and had taken a phenolphthalein laxative daily for many years. For an unspecified period of many years he had been edentulous, and he had not recently used dentures because of soreness of his gums.

Physical examination showed a well-developed and well-nourished man with dry lips and skin. The gums were swollen, reddened and hypertrophic. No masses or tenderness could be made out in the neck. The lungs were normal. The cardiac apex impulse was neither seen nor felt but the heart did not seem to be enlarged. The sounds were of good quality and there were no murmurs. The rhythm was regular. The abdomen was soft, without spasm or tenderness. One examiner recorded a questionable mass just below the xiphoid. There were bilateral, reducible inguinal hernias. The prostate was slightly enlarged but soft.

The blood pressure was 146 systolic, 92 diastolic. The temperature, pulse and respirations were normal.

Laboratory studies showed a urine with a specific gravity of 1.020 and no albumin or sugar. Blood examination showed a red-cell count of 4,300,000 with a hemoglobin of 78 per cent. The white count was 9500, and the differential showed 84 per cent polymorphonuclear leukocytes, without other noteworthy features. The blood protein was 6.3 gm. and the nonprotein nitrogen 20 mg. per 100 cc. The blood chlorides were 104.6 milliequiv. per liter.

Fluid barium taken by mouth filled the hypopharynx and upper 2.5 cm. of the esophagus, dilating the latter. The barium then met an obstruction at the level of the manubrium, and repeated efforts at deglutition failed to force barium past this point. Spot films showed a rounded collection of barium approximately 2.5 cm. in diameter above this point of obstruction.

The day after entry a biopsy was performed on the hypertrophic gum and an esophagoscopy was done. At the junction of the upper and middle thirds of the esophagus, 18 cm. from the anterior tooth line, an obstruction was encountered. There the mucous membrane was thrown into puckered folds but showed no break or ulceration. Soft bougies could be passed up to and including a No. 24. The esophagoscope did not pass. Several bits of tissue were taken for biopsy. Histologic examination of the two sets of specimens showed chronic gingivitis and no abnormality of the esophageal mucosa.

Following instrumentation the patient coughed up some "bloody pus" and thereafter found it easier to swallow liquids. On the fifth day a Beck–Jianu gastrostomy was done. Exploration of the upper abdominal cavity was negative. Following operation he seemed comfortable, and his temperature remained normal. The chest was clear except for a few moist rales at both bases. On the morning of the fourth postoperative day he complained of generalized discomfort which he was unable to localize. Examination showed slight abdominal distention, and the abdominal wound was found to have eviscerated to but not through the skin. The lips were cyanotic. The

blood pressure was 125 systolic, 80 diastolic, and the pulse 100. The heart and lung findings were unchanged. While being prepared for an enema the patient suddenly collapsed, became pulseless and deeply cyanotic, and expired.

Differential Diagnosis

Dr. Carroll C. Miller: Cases of obstruction of the esophagus can be considered under three common headings: diverticulum, stricture and carcinoma. Benign tumors of the esophagus are relatively rare; malignant tumors are of fairly common occurrence as tumors of the gastrointestinal tract go. Strictures may be congenital but more frequently they are traumatic and usually due to the scarring caused by a caustic solution taken with suicidal intent or by accident. Carcinoma of the squamous-cell type is the usual malignant tumor.

We have here an elderly man with no symptoms of difficulty previous to ten years before he was first seen. At that time he began to have obstruction of the esophagus. The symptoms at the time of the first episode are a little confusing. It is said that he had "dyspepsia," which might be indigestion or perhaps heartburn or pain in the upper abdomen. He had slight pain in the pit of his stomach and considerable gas but no nausea or vomiting. Later on the record states that there had been no regurgitation or vomiting. I am unable to relate this particular symptom of dyspepsia to what subsequently developed, except by a referred influence on the motility of the stomach or encroachment on the wall of the stomach by some process above. I am not inclined to attach much significance to this symptom, except that perhaps it was the earliest, simplest sign of trouble higher up. Often, however, patients with tumor of the esophagus have no indigestion.

The x-ray diagnosis of "fallen stomach" probably has no significance, especially in light of the abdominal exploration that was done later. We are fortunate in being able to look back on the whole picture rather than part of it, as the original clinician had to do.

The question of esophageal diverticulum is an interesting and important one. There are some points about the case that strongly suggest a diverticulum of the esophagus. Diverticulums occur in three parts of the esophagus, most frequently in the upper esophagus just below the hypopharynx. These are called pulsion or sometimes traction diverticulums. The next commonest are in the middle half or upper middle third, in the region of the bifurcation of the trachea, and finally but rarely they occur in the lower portion, where the muscle fibers start to thin out to become the cardia of the stomach. A patient with an esophageal diverticulum in the upper third often complains of something sticking at the region of the larynx. This may be due either to the lodgment of food particles in the entrance to the diverticulum or to filling of the diverticulum and compression of the esophagus, causing obstruction of the main lumen. A similarly significant symptom is the story of rubbing the neck from above downward to get rid of the food. This is frequently done by patients with diverticulum of the upper part of the esophagus. The pouch is low in the neck and by massaging that pouch the material contained therein can be expressed and deglutition can progress normally. We have no progression in this case for approximately two years. I assume that the patient was going on with the same general schedule of eating soft food, of massaging his neck and of having occasional bouts in which food stuck in the neck above the larynx; suddenly he became unable to swallow anything more than saliva and water.

On physical examination there were no clinical signs of a malignant process, and the x-ray findings were also negative. Patients with carcinoma of the esophagus frequently show loss of weight because of the difficulty in eating. We have no x-ray signs that could be called conclusive of carcinoma or tumor of the esophagus. The changes in the mouth — the red and swollen hypertrophic gums — were undoubtedly due to vitamin deficiency. This man probably was not getting his full quota of vitamins. He was living on liquids and a rather limited variety of them.

There were some rather interesting x-ray studies, and we might look at the films at this point. The barium taken by mouth filled the hypopharynx and the upper 2.5 cm. of the esophagus, dilating that part of the esophagus.

Dr. Richard Schatzki: When one looks at the x-ray films there are a few things that may be added to the report in the record. One is the fact that the obstruction apparently was unusually complete. In none of these films do I see any barium beyond the plane of obstruction. Because of the marked obstruction there was some spilling of barium into the larynx and the trachea. The other point which may be added is that the round shadow is fairly smooth in outline but is irregular at the lower border in all the films, which may be due to tumor or may be due to food. I think from the evidence we have here it is impossible to say which of the two it is.

DR. MILLER: This pocket of barium is at the level of the manubrium as stated in the report, is it not?

DR. SCHATZKI: That is correct.

DR. MILLER: As I understand the topography of the esophagus that level is less than 18 cm. from the anterior tooth line as measured in esophagoscopy. Would that agree with the 18-cm. mark?

DR. RICHARD SWEET: I think it would agree, from the tooth line.

DR. MILLER: I had the impression that the obstruction seen by esophagoscopy was lower. Now I see that this is a well-rounded barium shadow.

DR. SCHATZKI: There is one lateral film, which may have significance. This is the filled hypopharynx, and you can see the round accumulation of barium about which we are talking. Between the two there is narrowing. It may be coincidental and transient, or it may be the neck of something. I do not know. You can see the same appearance in the anteroposterior view. On the other hand it seems to lie in the midline.

DR. MILLER: The fact that it lies in the midline is rather against a diverticulum because usually they are pressed to one side or they protrude from behind the esophagus so that they extend from the esophagus laterally. There was obviously some degree of dilatation of the esophagus from prolonged obstruction. The esophagoscopy showed an obstruction, which apparently extended all the way around the esophagus. I judge from the report that the esophagus was puckered and folded in its entire surface but showed no break or ulceration. An interesting fact is that bougies could be passed up to and including No. 24, which is a moderate size, thus showing that a certain amount of dilatation was possible, but not enough to allow the esophagoscope to pass.

The patient then had an episode indicative of sepsis. Bloody pus was coughed up, and at that point it was easier for the patient to swallow liquids. The medical attendants obviously thought that surgery was warranted, and exploration was done abdominally. Apparently no abnormal lymph nodes or no abnormality of the stomach itself was found, so a Beck–Jianu gastrostomy was done. For four days the patient seemed to do well but suddenly had a bad turn, the nature of which is indeterminate except for the fact that inspection of the abdominal dressing showed that he had an evisceration through the inner layers of the abdominal wall; then came a sudden collapse.

I have a feeling that this man must have had a carcinoma of the esophagus that perforated. The pouch seen in the x-ray film represents either an abscess cavity or a dilated esophagus above the point of constriction, which Dr. Schatzki pointed out. The instrumentation of the esophagus stirred up the infective process in the abscess cavity so that the patient coughed up bloody pus, the product of the degeneration that had occurred there. The nature of the terminal episode I cannot be sure of, and it is not particularly important in the present diagnostic problem. It may have been a cerebral embolus, or it may have been a coronary attack. We have no data to indicate whether there were any symptoms of explosive cough which might indicate rupture of an abscess or tumor into the bronchial tree and cause the patient to become deeply cyanotic. Deep cyanosis can occur either with cerebral embolus or with sudden obstruction to the air passages. My diagnosis is carcinoma of the upper third of the esophagus with abscess formation.

DR. TRACY B. MALLORY: This case somewhat resembles a case you discussed recently, Dr. Lerman. How do you feel about this one?

DR. JACOB LERMAN: I am impressed by the fact that the x-ray films did not show irregularity of the esophageal wall, which is usually present with carcinoma of the esophagus.

DR. SCHATZKI: There is some irregularity.

DR. LERMAN: The description is not that of an ulcerative lesion. At least you did not mention it when you discussed it.

DR. SCHATZKI: It is irregular, however.

DR. LERMAN: Would you say it was ulcerated? The esophagoscopist did not describe ulceration. Since the two methods of examination seem to agree I should say that that is an important argument against it. Is there evidence of an extrinsic lesion pressing on the esophagus?

DR. SCHATZKI: None is visible.

CLINICAL DIAGNOSES

Carcinoma of esophagus.
Coronary occlusion?

DR. MILLER'S DIAGNOSIS

Carcinoma of the esophagus, with perforation and local abscess formation.

ANATOMICAL DIAGNOSES

(Cardiospasm.)
Esophagitis, acute, ulcerative.
Gastritis, acute, with pseudopolyposis.
Bronchopneumonia.
Pulmonary edema.
Pulmonary congestion.
Hydrothorax, bilateral.
Hydropericardium.
Cardiac hypertrophy, hypertensive type.

Arteriosclerosis, marked coronary and moderate aortic.
Nephritis, chronic vascular, slight.
Cortical cysts of kidney.
Operative incision: gastrostomy.
Incisional hernia.

Pathological Discussion

Dr. Mallory: The autopsy was done with the esophagoscopist present. He readily passed his instrument at the autopsy table, meeting no obstruction. On removing the esophagus we found that the first 1.5 cm. of the esophagus was normal. Below that point the wall was edematous and three or four shallow, apparently acute ulcerations were present in the esophageal mucosa. From there on down to the cardia the esophagus was markedly dilated and the wall extremely thickened, so that in spite of the fact that this story had from beginning to end suggested obstruction at the level of the larynx, all the anatomic evidence clearly points to chronic obstruction for many years at the level of the cardia. There was nothing anatomic to explain chronic obstruction in the upper part of the esophagus. It is an extremely odd story for cardiospasm, and yet that is the only diagnosis that is consistent with the anatomic findings.

Dr. Schatzki: You assume that he had spasm in the region of the acute ulcer?

Dr. Mallory: The facts that during life the esophagoscope would not pass and that after death it passed easily indicate to my mind that the obstruction must have been spastic.

Dr. Lerman: The ulceration and gingivitis could be consistent with a deficiency syndrome.

Dr. Mallory: Yes. This is the second case we have had here in a month of benign ulceration accompanied by symptoms of stenosis in a patient with generalized vitamin deficiency. Since we published the first case[1] my attention has been called to a paper by Merrill and Richards[2] from the Pondville Hospital. They report three cases referred to the clinic as cases of carcinoma of the esophagus because of dysphagia, obstruction and even x-ray findings suggestive of carcinoma that were cured by intensive vitamin therapy. In these cases objective evidence of neuritis of the ninth and tenth cranial nerves was obtained.

Dr. Miller: Does this round x-ray shadow represent ulceration through the wall and a pocket behind it?

Dr. Mallory: No; the ulceration was only 1.0 mm. deep. This is simply localized dilatation above a point of stricture.

The terminal episode was massive pulmonary edema with a considerable grade of hydrothorax attributable to acute circulatory failure.

Dr. Sweet: There are two points that ought to be mentioned in regard to this patient. On the wards we thought he had carcinoma.

We have learned in recent years the vast importance of a diagnosis of esophagitis. In our experience, it is much more frequent in the lower third or quarter near the cardia than higher up. I have run across it in the differential diagnosis of carcinoma several times, and it is a significant finding.

Furthermore, I have acquired this impression about biopsy. If the biopsy specimen shows only an inflammatory process with x-ray evidence that looks like carcinoma in the upper portion of the esophagus, the lesion is unlikely to be carcinoma. In the lower portion of the esophagus it is likely to be a carcinoma that has grown up from the stomach into the esophageal wall with a submucosal extension. In such cases the esophagoscopist may obtain only mucous membrane, the carcinoma lying deeper. I doubt if that happens commonly, although within two weeks we had a case in which an esophageal carcinoma opposite the manubrium was diagnosed with difficulty. The first biopsy showed chronic inflammation, and the second tumor. I have the impression that this discrepancy does not occur so frequently in high lesions as it does in lower ones, but we must be on the lookout for the diagnosis of esophagitis at any level. I have seen several cases.

Dr. Mallory: It is of great practical importance not to assume that a case of this sort has carcinoma of the esophagus and is therefore hopeless.

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CASE 29122

Presentation of Case

An eighty-year-old retired grocer entered the hospital because of severe abdominal pain and constipation.

The patient was quite well until ten days before admission, when he became constipated despite the daily use of mineral oil. Five and a half days later he had two small bowel movements. The stools were brown but firmer than normal. Three days before entry he became slightly distended and developed generalized crampy abdominal pain. Several hours later he began to vomit a brownish fluid. The vomiting and pain continued unchanged to the time of admission. There was no pyuria, hematuria, chills, fever, jaundice, acholic, tarry or bloody stools.

The family history was noncontributory. For many years the patient had had an easily reducible left inguinal hernia, which a truss kept satisfactorily reduced.

Physical examination revealed a thin man who vomited frequently. The skin and mucous membranes were dry. The tongue was beefy red and dry. The chest was emphysematous, and the percussion note hyperresonant. A soft systolic murmur was audible at the apex. The abdomen was markedly distended, and the umbilical dimple flattened. Peristaltic waves were occasionally seen crossing the abdomen in the epigastrium and right lower quadrant. There was marked tympany over the entire abdomen. Only peristaltic rushes and loud borborygmi were audible, and these were loudest in the right half of the abdomen. There was generalized tenderness and rigidity. A large left direct inguinal hernia was easily reducible and was not tender. Rectal examination was not remarkable.

The blood pressure was 160 systolic, 75 diastolic. The temperature was 97.4°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,400,000 with a hemoglobin of 70 per cent, and a white-cell count of 8100 with 62 per cent polymorphonuclear leukocytes. The urine was normal. A blood Hinton test was negative. A roentgenogram showed that the abdomen was filled with gas-distended loops of small bowel; one loop in the pelvis had somewhat the appearance of sigmoid. The only air in the colon seemed to be in the rectum, which was not distended. Several hours after admission a barium enema readily filled the large bowel and revealed no abnormality.

Parenteral glucose and saline infusions and citrated-blood transfusions were administered, and a Miller–Abbott tube passed. The latter passed to the cecum and decompressed the dilated loops of small intestine.

On the ninth hospital day the Miller–Abbott tube was pulled back from the cecum for about 30 cm. into the ileum. Barium that was passed through the Miller–Abbott tube showed a slightly but definitely dilated ileum. There was a sudden narrowing of the ileum beginning about 15 cm. proximal to the ileocecal valve, and there was marked peristalsis of the ileum proximal to the point of narrowing. The amount of barium pushed through the terminal ileum was small, but the greater part of this portion of the ileum was seen to widen out at one time or another. An area approximately 2.5 cm. in length at the beginning of the narrowed ileum never showed distention; the mucosa in this area seemed to be preserved. There was a similar area closer to the ileocecal valve, which showed some rigidity.

An operation was performed on the tenth hospital day.

Differential Diagnosis

Dr. Leland S. McKittrick: May we see the x-ray films? Be very careful what you say, Dr. Holmes, because a great deal depends on you.

Dr. George W. Holmes: This is the type of problem where the man who did the examination had a much better chance than I have. Furthermore, it is the type of case that the radiologist needs about an hour's study before making any real statement. I am saying this so that I will not mislead you, because anything I say will probably be wrong. There are, however, a few things that are obvious.

At the time the barium enema was given, the patient had a tremendously dilated small bowel and some gas in the large bowel; it does not look as if he had any gross pathology in the large bowel. I think we can agree with the man who made the examination that the lesion was low in the small bowel and close to the cecum. His description is rather better than anything that I can give you.

Dr. McKittrick: The cecum is normal?

Dr. Holmes: Yes. So far as I can tell the lesion was in the terminal ileum or outside the bowel involving the cecum, such as an appendiceal abscess.

I am surprised that the Miller–Abbott tube did not deflate the bowel. Even with the tube in place there was still a good deal of gas. They took a film of the chest, which I should say was normal for a man of his age.

Dr. McKittrick: We must start with the supposition or premise that this man had small-bowel obstruction. I do not believe it is possible to have the amount of dilated small bowel he had from a lesion in the large bowel, and in addition to that we have the confirmation that was given by the passage of barium from the rectum to the cecum, which showed a normal large bowel. Therefore we start with the premise that this man of eighty entered the hospital with small bowel obstruction. That may not be correct, but it is the only diagnosis we have any right to make.

If we start with the argument that he had small-bowel obstruction, what was the cause? I am perfectly frank to confess that I can talk myself out of any diagnosis that I wish to make. The only evidence we have is that the obstruction was in the terminal ileum. That is all right so far. Then the problem is, What was the nature of this man's obstruction? It seems to me there are a

couple of ways of approaching it. He could have had intrinsic cause of obstruction, that is, a tumor or an inflammatory lesion. If it was a tumor, it was probably either a carcinoma, a lymphoma or possibly a leiomyosarcoma; if it was an inflammatory lesion, it was probably either tuberculosis or enteritis. The only other intrinsic type of lesion is foreign body, and I do not think we need give much time to that. If it was not intrinsic, and I do not believe that we can say definitely that it was intrinsic, then it could have been extrinsic, as Dr. Holmes has said. The likeliest extrinsic lesions are an inflammatory process, such as appendiceal abscess, an adhesive band, the most frequent cause of acute small-bowel obstruction, and a tumor in an adjacent structure pressing from outside. It seems to me that somewhere in that list is the explanation for this man's disease.

Let us consider an adhesive band, which is the most frequent cause of obstruction. I shall be greatly disappointed if he had such a lesion. From the history, if it is correct, the first symptom he had was constipation. No one with acute small-bowel obstruction due to an adhesive band has a right to have constipation as the first symptom. The first symptom in 95 per cent of these cases is pain. Since this patient had constipation for three or four days before he had pain, it is impossible for me to accept that diagnosis, and I cross a line through it.

What about an inflammatory process? That is the thing on which I have been trying to get Dr. Holmes to help me out. He has done the best he could. Did this old man have appendicitis?

DR. HOLMES: I might give more help by interpreting what is in the record. It says that the mucosa appeared to be intact. That would make one think the lesion was outside the bowel. Then it says that the lumen changed considerably in size.

DR. MCKITTRICK: All except one place.

DR. HOLMES: Yes, but that changed a little, as I read it.

DR. MCKITTRICK: Let us make sure of the quotation. "An area approximately 2.5 cm. in diameter at the beginning of the narrowed ileum never showed distention." I interpret that to mean there was a place 2.5 cm. long that stayed as it was.

DR. HOLMES: Perhaps that is a better way of interpreting it. At any rate I believe they were thinking of something outside the mucosa.

DR. MCKITTRICK: Of course this question of appendiceal abscess is of greatest importance. Could this man have such a lesion? One teaching that we have always been brought up to believe is that appendicitis in an old man is a queer disease and never gives the classic picture. It comes when we least expect it. I was hopeful that something in the x-ray report would indicate a pressure defect on the cecum to suggest that this man did have an appendiceal abscess. At the moment I shall put a question mark beside this diagnosis.

Next is the question of intrinsic inflammation. Could this man have had a process in the wall of the bowel itself that had left the mucosa intact? It seems to me that if he had had regional enteritis, tuberculosis or anything of that sort he would have had some symptoms prior to ten days before admission. I do not believe one is entirely safe in excluding such a process because the history is short, but it does seem that the history is too rapidly progressive for that type of lesion. I am unwilling to accept either regional enteritis or tuberculosis as the cause of this man's trouble, and I shall cross them out.

Then we come to the group of tumors. Did the patient have carcinoma, lymphoma or leiomyosarcoma? Again, the story is too acute and rapidly progressive for carcinoma of the terminal ileum, unless it had intussuscepted. If it had, the initial symptom, I think, would have been pain and not constipation. So you see, I can talk myself out of everything I can think of. We can possibly attach some significance to one statement of the X-ray Department, namely, that the mucosa in this area was intact. If the mucosa was intact, the lesion could not have been cancer. It probably was not lymphoma. So I cross a line through that group, and that brings me back to the question of an external inflammatory process.

Was this appendicitis? I cannot answer the question. I do know this—there is nothing in the story inconsistent with it. Appendicitis can result in secondary obstruction. I do not know how much attention to pay to the widespread rigidity and tenderness. I do not know whether the subnormal temperature means anything, but I do not believe it does. The white-cell count and differential mean nothing. The patient was eighty years old, and a person may have appendiceal abscess at that age. I shall have to say that he had small-bowel obstruction, that the lesion was probably extrinsic and that the likeliest extrinsic lesion is an inflammatory process, probably originating in the appendix.

DR. E. PARKER HAYDEN: I should like to ask Dr. Holmes if lymphoma can be excluded on the lack of destruction of the mucosa. I believe that a normal mucosa can be found with lymphoma.

DR. HOLMES: That is true, but an ulcerative lesion can also be present. If one is trying to decide between carcinoma and lymphoma, and

if the mucosa is intact, the lesion is a little likelier to be lymphoma. Perhaps Dr. Mallory can answer that better than I can.

DR. TRACY B. MALLORY: There is one other neoplasm in this area that should be considered more seriously than those two, that is, carcinoid. The mucosa is never ulcerated with a carcinoid, but I think the pattern might be altered.

DR. MCKITTRICK: Do they occur in the terminal ileum?

DR. MALLORY: Yes; next to the appendix that is the favored spot, and I have seen one in an eighty-year-old man.

CLINICAL DIAGNOSIS

Mucocele of appendix, with mechanical obstruction.

DR. MCKITTRICK'S DIAGNOSIS

Abscess of appendix, with secondary small-bowel obstruction.

ANATOMICAL DIAGNOSIS

Mucocele of appendix, with mechanical obstruction.

PATHOLOGICAL DISCUSSION

DR. NATHAN D. MUNRO: After the Miller–Abbott tube was in place, the general pain, tenderness and spasm subsided. The patient later developed an indefinite tenderness in the right lower quadrant. The x-ray films were of considerable help. The differential diagnosis was much as Dr. McKittrick suggested. Dr. D. N. Sweeny operated and found a mucocele of the appendix, which was reported to show subacute inflammation. It was adherent to the terminal ileum and was evidently the cause of the obstruction.

DR. MALLORY: Before it was opened the mucocele was sufficiently distended to make a small but significant tumor mass.

DR. MCKITTRICK: May I add that I got the greatest satisfaction out of reading this case over because of the way it was handled. Here was an eighty-year-old man with small-bowel obstruction and distention who undoubtedly would have died promptly after an emergency operation. The passage of a Miller–Abbott tube, with relief of distention, and later x-ray visualization of the obstructed area were just the things to have done.

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PROPAMIDINE—A NEW WOUND ANTISEPTIC

A recent issue of the *Lancet* focuses attention on a new antibacterial agent for topical application in infected wounds. In a study of the effect of the aromatic diamidine series on protozoa Fuller[1] noted that propamidine (4:4′ diamidino-diphenoxypropane dihydrochloride) also possessed an antibacterial effect. This substance has been carefully studied by Thrower and Valentine,[2] because its bacteriostatic action is not inhibited by peptones, tissue fluids, pus or para-aminobenzoic acid. The lowest concentration of propamidine showing a clear bactericidal effect on hemolytic streptococci in pus was 0.003 to 0.005 per cent. For staphylococcal pus the effective concentration was 0.025 to 0.050 per cent. Studies of broth cultures suggested that the anaerobic gas-producing bacilli were about as sensitive as staphylococci. In vitro phagocytic tests performed with defibrinated blood and staphylococci showed that phagocytosis was practically unaffected by 0.1 per cent propamidine, slightly reduced by 0.2 per cent and inhibited by 0.4 per cent. Even in a concentration of 0.4 per cent the leukocytes were not killed and the red cells were not hemolyzed. Thus it would appear that bactericidal concentrations of the drug are well below the cytotoxic level.

A clinical technic for the application of propamidine to wounds was evolved by trial on patients with osteomyelitis, infected burns and septic wounds of the soft parts. The wounds are cleansed with physiologic saline solution and are surgically exteriorized by incision, if necessary to ensure adequate contact of the drug with all infected surfaces. One tenth per cent propamidine in a base consisting of 4.5 per cent methyl cellulose in water is applied as a jelly to the wound surface and sealed over with vaseline gauze. The wound is dressed and similarly treated on alternate days for a total of five treatments. Care must be taken to avoid contact with the intact skin lest it become inflamed and irritated by the jelly. Treatment for more than ten days or concentrations above 0.1 per cent have led to superficial necrosis of the granulation tissue. It is apparent that the full antibacterial effect is readily obtained within the ten-day period. Streptococci disappear first and are followed by staphylococci. Proteus and pyocyaneus bacilli usually persist but do not appear to retard healing. Wounds with persistent sinuses or incomplete healing after the ten-day period of treatment are judged ready for operative removal of foreign bodies, sequestrectomy or skin grafting.

Propamidine jelly was released for trial at an EMS hospital in 5 cases of infected ulcer and casualty wounds and 8 cases of burns.[3] The infected ulcers and wounds became sterile, or nearly so, in four to ten days and thereafter healed rapidly or were successfully grafted. The burned patients were relieved of pain, second-degree areas

healed within ten days, and infection did not occur. Morley and Bentley[4] obtained similar results in 7 cases of recent burn and are of the opinion that propamidine was effective in the treatment of older burns infected with sulfonamide-resistant organisms.

McIndoe and Tilley[5] used propamidine jelly in 11 patients with secondary hemolytic streptococcus infections of wounds and burns not improved by local applications of Eusol and sulfanilamide or by saline dressings. Recently infected wounds cleared more rapidly than older ones, but the streptococci disappeared from all within the ten-day period. In 3 cases there was partial loss of subsequent skin grafts from staphylococcal infection.

It is to be hoped that further trial of propamidine will confirm these encouraging reports. There can be little doubt that the drug will be exhaustively studied in the near future. No success has attended the intravenous use of propamidine in experimental streptococcal infections in mice.[1] Furthermore, clinicians will do well to note that drugs of this series have produced circulatory collapse or violent itching after the intravenous injection of 2 mg. per kilogram of body weight for sleeping sickness.[6] It seems likely that absorption of topically applied propamidine will be slight, but this is an inference from the behavior of the related and fluorescent compound, stilbamidine,[7, 8] which is stored in the liver and kidneys and is absorbed by the red blood cells. The possibility of immediate and late toxic effects is apparent. Until more experience has been gained it is unwarranted to use the drug for large wounds or in patients with impending shock.

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BOSTON'S AMPHIBIAN HOSPITAL

A SEA-GIRT country such as ours can boast of more than one floating hospital—of which the Navy's hospital ships are the present outstanding examples; only Boston can boast of an amphibian hospital that has breasted the unruly ocean for season after season, and finally climbed onto the land, not to rest but there to continue its labors. A unique Boston charity, the Boston Floating Hospital has now dropped the limitations imposed by the pure charitableness of its nature and has made its facilities available to those who can pay.

The Boston Floating Hospital was largely the product of the labors of the Reverend Rufus P. Tobey, who, with the aid of Edward Everett Hale, Dr. Francis P. Brown and others, chartered the barge *Clifford* in 1894. In the summer of that year the boat made five excursions down the harbor, bearing mothers and their ailing offspring for a day's outing. In the following year the *Clifford* was purchased and daily trips were made; and in 1896 the barge was transformed into a real hospital ship, with permanent wards, attending physicians and a training school for graduate nurses. In 1906 the *Boston Floating Hospital*, as a generation of pediatricians knew her, was built, and for twenty-one years continued her voyages of mercy with her cargoes of sick babies from the North End, the West End and the South End. There, also, important work was done in the study of infectious diarrhea and in the development of suitable foods for infants. The ship burned in 1927, and owing to less need for a hospital of this sort, largely because of the great decrease in the incidence of summer diarrhea, it was decided not to rebuild her. She had performed a great service.

Then the amphibian nature of her character was revealed, for out of her ashes, phoenixlike,—and after a dormant period passed in the vicinity of the Harvard Medical School,—came a metamorphosed and thoroughly landlubberly Boston Floating Hospital, entirely rid of the tang of the sea, primly and with the utmost stability associated with the Tufts College Medical School and the

Boston Dispensary to form the New England Medical Center. In 1931 the new ship, of stone and brick and concrete, was warped into place beside the remodeled Boston Dispensary; and there she lies, high and dry and thoroughly free of barnacles.

Dr. Henry I. Bowditch was for many years physician-in-chief of the seagoing floating hospital; Dr. Elmer W. Barron presided over its terrestrial destinies until the fall of 1942, when Dr. James M. Baty took up the post by the binnacle. And now, at last, patients are to be allowed to help pay their own way, and they will not have to go aboard by a gangplank.

OBITUARY

ELLIOTT GRAY BRACKETT
1860–1942

To appraise adequately the loss of one who has for so many years served the public in so many ways and accomplished it so unobtrusively, unselfishly and untiringly as did Elliott Gray Brackett, cannot be done by any one person. His character was a jewel of many facets and it mattered not from what angle it was viewed, nothing but serenity, understanding sympathy, and quiet, tireless devotion to the tasks that were before him were reflected from it.

His was a life of unstinted devotion of all his talent to the service of his patients. His records reveal how meticulous he was to note every material fact bearing on the conditions he was called on to treat. No detail was too trivial to attract his attention, and in his effort to arrive at a true estimate of the significance of reported symptoms he did not confine himself to physical signs. To an unusual degree he acquired an understanding of the bearing of seemingly wholly extraneous circumstances that often exerted a psychic influence over the purely physical complex. In his association with patients he so invariably convinced them of his complete absorption in their problems that they were impressed by the feeling that they were not merely "another case," to be dealt with in the routine way, but deserved the utmost of his skill to unravel their difficulties and provide the most appropriate treatment. To this initial care he added a "follow-up" that left no doubt in their minds that he was wholeheartedly concerned with their progress toward recovery.

No one who was privileged to work with him could fail to appreciate the value of this attitude toward the practice of a profession. This would probably be particularly true of the specialty to which he devoted his life, where so much depends on attention to minutiae in dealing with conditions which are usually chronic and involve to an unusual degree the maintenance of a morale essential to success. And so it was that the organization of his office was such, over many years, that it reflected the spirit which motivated him and helped in the achievement of the goal for which he strove. It mattered not to him what the social statuses of his patients were, whether he met them in an outpatient clinic or they came to him as private patients; they commanded the complete absorption of his attention.

As an instance of this, during the last day of his life he had his mind so much on his patients' welfare that he had his shopman bring to his bedside a brace he had planned, in order that he might see that it had been made as he wished it to be.

Because he was a past master in the fitting of apparatus, he used braces and other means of support to a greater extent than many present-day practitioners. He did excellent surgery when he thought surgery was indicated, but was never hurried into it before he had reason to think it would be the opportune time. I imagine it would be the consensus among those who worked with him as assistants over any considerable period that his judgment of the proper time to resort to operative surgery and his ability to control patients until that time arrived were, in the first respect, sound, and, in the latter respect, no less remarkable. His familiarity with the literature of his specialty and his acquaintance with its ablest exponents served to make him "not the first by whom the new is tried, nor yet the last to lay the old aside." In other words, though conservative, based on his experience, he was open-minded to the last years of his activity.

To appreciate the esteem in which he was held by all who had been under his care, one should see the many letters that have come from his former patients. And it was not only from those whose association with him had been that of patient with physician; there are numberless letters from physicians who, at one time or another during their student years, had come under the spell of his influence. He had a way of impressing his personality on them which prompted many of them to feel that he had influenced their whole lives, inspiring them with his ideals and compelling them to make acknowledgment of their indebtedness to him.

He had unusual opportunities to make such contacts because of the many positions he occupied where younger men were brought into relation with him. A long service at the Children's Hospi-

tal in Boston, at the House of the Good Samaritan and the Boston City Hospital, followed by the headship of the Orthopedic Service at the Massachusetts General Hospital, and latterly at the Faulkner Hospital, brought him in contact with many undergraduate medical students, interns, residents and graduates taking refresher courses, from all over the country. In addition, his position since 1922 as editor of the *Journal of Bone and Joint Surgery*, the official organ of the American and the British orthopedic associations, made him acquainted, often quite intimately, with the leaders of thought and clinical activity the world over.

All these contacts, through clinical channels as well as by virtue of his journalistic work, served to keep him abreast of what was going on in the orthopedic world. The organization of the American Academy of Orthopaedic Surgeons and its affiliation with the *Journal of Bone and Joint Surgery* have added many new contributors to that journal and consequently have widened his acquaintance with several hundred younger men, now actively engaged in practice, who are the coming contributors to official orthopedic publications.

It was his custom for many years to take at least a two months' holiday in Europe, and while there he availed himself of the opportunity to attend meetings of orthopedic societies in various countries on the Continent and in the British Isles. It was at these gatherings that he succeeded in arousing interest for the journal in many foreign countries, where there are now a considerable number of subscribers, and even contributors.

His visits to Europe almost always found him centering his activities from Geneva, and it was there that he became an interested student of the questions that the League of Nations was attempting to solve. In fact, he took the necessary courses at Geneva to earn the League's diploma. He felt strongly that the future of the world's peace, as well as social and economic security, is dependent on some organization comparable to that for which the League was striving.

Honorary membership in many foreign orthopedic societies came to him as a result of his frequent attendance at their meetings and of his position as editor of the *Journal of Bone and Joint Surgery*.

Here in Boston his influence has been actively felt in such organizations as the School for Crippled Children and the Society for Occupational Therapy. He was a member of the Boston Orthopaedic Club and the Boston Surgical Society. The R.C.R.C. (Roxbury Clinical Record Club) had Dr. Brackett as one of its originators. He was a member of the Massachusetts Medical Society, the American College of Surgeons and the Vermont State Medical Society. He served as chairman of the Professional Committee of the International Society for Crippled Children.

In the American Orthopaedic Association there was no one more universally respected. For several years he was treasurer of the society, and its president for one year; but beyond doubt his greatest service was rendered during the twenty years that he edited its journal, now the outstanding publication devoted to orthopedic surgery.

During World War I he was called to the Surgeon General's Office in Washington to head the orthopedic branch of the Expeditionary Force, selecting and allotting members of that specialty to service abroad or in this country. Later he was sent overseas, where he spent considerable time near the front, returning with the rank of colonel in May, 1920.

The Rockefeller Foundation, learning that Dr. Brackett was thinking of visiting China, invited him to give a course of lectures to the medical students at Peking Union Medical School and to demonstrate the methods of treatment employed in American clinics. At Shanghai and at Shantung Christian University were located two of his former house officers, with whom he spent some time.

These are without doubt not all the channels through which he quietly made his influence felt, for ostentation was foreign to his nature.

He showed few indications of any toll that advancing years and an almost lifelong handicap to his physical activities had imposed on him. I never heard him refer to this handicap.

Although in all the years I knew him he never gave expression to any conviction he may have had on religious matters, he stands out in my thought as the nearest approach to the ideal Christian gentleman — the exemplar of the Great Physician. The philosophy of his life would find some parallelism in the following quotation:

> To live; to love; to die; to live again;
> This is the all of being; but how large
> Looms that adventure in the afterward!
>
> Nor life, nor love may here survive, but there
> Shall both endure, nor by endurance lose
> Their zest. New opportunities for use,
> New scenes, new joys, a sense of gratitude
> For things mysterious made manifest
> Shall there be mine, and not a thought intrude
> Regretful of the past. My soul awaits
> Expectant the transition. Do I hear
> The plash of Charon's oars?
> Ho! Ferryman
> This way!

C. F. P.

MEDICAL EPONYM

Tawara's Node

Dr. Sunao Tawara (b. 1873), working in the laboratory of L. Aschoff in Marburg, presented the results of his studies, covering a period of two and a half years, in a monograph entitled *Das Reizleitungssystem des Säugetierherzens. Eine anatomisch-histologische Studie über das Atrioventrikularbündel und die Purkinjeschen Fäden* [The Conduction System of the Mammalian Heart: An anatomicohistologic study of the atrioventricular bundle and the Purkinje fibers] (Jena, 1906). The node is described on pages 183 and 184 as follows:

> The system uniting auricle and ventricle forms a complicated muscular network of relatively large dimensions in the region just above the fibrocartilaginous atrioventricular septum, which we have termed a node. In one direction there courses from this node posteriorly a short bundle of fibers, arranged in a more or less parallel fashion, as far as the anterior portion of the coronary sinus, where it unites with the ordinary fibers of the auricle. In the other direction the node extends forward, growing rapidly smaller, to the ventricular portion and enters the ventricular septum after penetrating the fibrocartilaginous septum.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Breech Delivery: Resultant Injuries to the Nervous System

Injuries may occur to the peripheral nervous system, the spinal cord, and the brain during breech delivery.

Two portions of the peripheral nervous system may be injured, the lumbosacral plexus and the brachial plexus. Rather rarely traction on the legs, while the infant's body is still firmly held in the mother's birth canal, can produce injury to the lumbosacral plexus, with flaccid paralysis of the legs and sphincters and subsequent atrophy of the thigh and gluteal muscles. Subluxation of one of the lower lumbar vertebras has been occasionally demonstrated in such cases.

Traction on an arm or shoulder, with the head fixed in the mother's pelvis, may injure the brachial plexus. Tearing of the plexus from above downward usually occurs, so that the injury is likely to be severest in the nerve roots or trunks derived from the fifth and sixth cervical nerves, with the brunt of the paralysis in the muscles of the shoulder girdle. Generally the whole arm is temporarily paralyzed at birth, and the paralysis is maximal immediately after birth. Occasionally the whole plexus is torn in such a delivery, and rarely the brunt of the injury involves the nerves of the hand. In a few such cases a history of an extended arm during delivery is obtained, and the inference is that the plexus was torn from below upward. Injuries involving the lower portion of the brachial plexus generally involve the cervical sympathetic trunk, often with the production of a complete Horner's syndrome.

Two modes of injury may affect the spinal cord. Owing to the fact that the infant's spine is more elastic than the contained spinal cord, traction on the infant's pelvis with the head fixed in the mother's pelvis results in stretching of the spinal column and rupture of the dura and spinal cord in the thoracic portion. This accident is reported to be accompanied by a loud snap. Flaccid paralysis and anesthesia below a given level, present immediately on delivery, are the usual signs. If a large enough segment of spinal cord is isolated below the injury, automatic sphincter and reflex phenomena in the legs soon develop. Incomplete rupture of the cord may be produced, with no complete anesthesia and with loss of motor power below the level of injury.

The spinal cord may also be injured by avulsion of the roots of the brachial plexus from the cord by traction on a shoulder or arm against a fixed head. The result is hemorrhage into the cord, with symmetrical flaccid paralysis of both arms, often more marked on one side, and with varying degrees of loss of sensation below the level of injury. If severe, such injuries are permanent. Minor injuries of this type accompany most brachial palsies and tend to clear spontaneously in a few weeks. There is some evidence to suggest that they may remain latent and in young adult life give rise to degenerative processes in the cervical spinal cord.

Injury to the brain during breech delivery results, at least in certain cases, from displacement of the cranial contents. Normally, the falx and tentorium act as supports for the brain, preventing its downward displacement into the foramen magnum. During breech delivery, traction on the already delivered trunk is transmitted to the spinal cord and puts the tentorium under strain. When suprapubic pressure on the undelivered head is added, the strain may be increased to the point where the tentorium ruptures. When this occurs the brain is displaced downward and the medulla herniates through the foramen, thus damaging the respiratory center. In addition, the vein of Galen is torn or angulated, and this interferes with the venous drainage from the basal region of the cerebrum. General fetal anoxemia results from the injury to the respiratory apparatus, and in

addition, especially severe injury may result to the region of the basal ganglia and other structures surrounding the third ventricle.

Finally, injury to the calvarium, with fracture or hemorrhage over the surface of the brain, may occur, usually as a result of suprapubic pressure or the application of forceps to the after-coming head. Such an injury may produce signs of intracranial distress, such as convulsions and asphyxia, at once, or if damage involves the cortex only, its effect may be apparent as hemiplegia, quadriplegia or mental defect as the baby develops.

The structure of the nervous system is well adapted to forces of compression exerted during labor, provided they are not continued over too long a period; but in general the nervous system cannot withstand the stresses and strains imposed by forces which tend to stretch the baby.

WAR ACTIVITIES

INDUSTRIAL MEDICINE

Dermatitis Investigation in Seattle Shipyards

The chloracne among electricians in Seattle shipyards, which caused considerable alarm and a threatened strike, was due to the type of cable used and the fact that the electricians handled it continuously, reported Dr. Louis Schwartz, who made the investigation. Only one shipyard had cases of chloracne. The three remaining yards used another type of cable and electricians spent only part of their time stripping.

The alarm and the threatened strike in the Seattle shipyards followed newspaper reports of a dermatitis outbreak and 3 deaths due to acute yellow atrophy of the liver among workers at the Anaconda Copper Company, Hastings-on-the-Hudson, New York. The Seattle electricians were handling wire made by the Anaconda Copper Company and some of them had developed a dermatitis that they attributed to handling the wire. They were finally persuaded to remain at work until someone from the United States Public Health Service could arrive and make an investigation. Dr. Louis Schwartz immediately flew to Seattle where he examined workers who had the so-called "cable rash" to determine if it was a chloracne.

The cable which caused the acne was found to be the Anaconda cable in which asbestos impregnated with chlorinated compounds is loosely packed and flakes off during stripping operations. Precautions recommended by Dr. Schwartz for handling this special Anaconda cable with the loose insulation are as follows:

(1) Workers engaged in stripping cable containing either chlorinated naphthalene, chlorinated diphenyl or chlorinated diphenyl oxide should be supplied with hood respirators. It is preferable to have these hood respirators made from a transparent synthetic resin, such as pliofilm or vinylite, or perhaps from a fireproof cellophane. The eyepiece should be a large flat plate of lucite rather than the conventional double lenses. The respirator should be closely fitted to the nose and contain such filters as will efficiently remove dust and wax.

(2) Workers should be supplied with clean overalls daily, the overalls to be laundered at the plant.

(3) Workers should wear long underclothes and change them daily.

(4) Workers should be required to take a shower before going home, and they should be furnished with toilet soap for this purpose.

If the hood respirator cannot be obtained or used, protective ointments of the type that coat the skin with a dry film and prevent the halowax from touching the skin should be applied to the face, neck and ears. Two such ointments are the tetryl protective cream developed by the United States Public Health Service, obtainable from the West Disinfectant Company, and a preparation Sav Skin No. 2, obtainable from the Doak Company, Cleveland, Ohio. These ointments should be applied before going to work, washed off before going to lunch, reapplied after lunch and washed off before going home.

At the end of the investigation, a meeting of the dermatologists in Seattle was called and 4 cases of chloracne were presented before them to acquaint them with the diagnosis and the recommended methods of treatment. — Reprinted from *Industrial Hygiene*, a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

PULMONARY TUBERCULOSIS RESULTING FROM EXTRAFAMILIAL CONTACTS

The possibility of the spread of tuberculosis within the family because of close contact cannot be too strongly stressed. The disease may attack as many as four generations. However, this should not obscure the importance of continuing the search for contacts outside the immediate household when case finding does not reveal the source of infection within the family. The importance of extrafamilial contacts is shown in a recent paper (Twinam, C. W., and Pope, A. S. Pulmonary tuberculosis resulting from extrafamilial contacts. *Am. J. Pub. Health* 32:1215–1218, 1942), from which the following is abstracted.

In mass surveys there is not the opportunity for individualization of cases that is necessary to discover extrafamilial sources of tuberculous infection. Rural communities with low death rates have afforded excellent opportunities for demonstrating the importance of extrafamilial contact in the spread of tuberculosis in the community.

In Massachusetts a five-year survey on the control of tuberculosis was recently conducted in a county considered to be representative of a rural New England community, and with next to the lowest death rate from pulmonary tuberculosis of any county in the state.

It was during this survey that attention was focused on the importance of extrafamilial contact. In March, 1935, and August, 1936, two cases of pulmonary tuberculosis were reported in a small community of approximately 4000 persons. Both cases were high-school girls, aged eighteen and sixteen respectively. They were the only young persons in their respective homes. Members of family A were examined and were found to have no evidence of tuberculosis. Family B refused examination at the time, but were subsequently examined and found to be negative for tuberculosis. There was no history of tuberculosis in either of the families. Both households used raw milk from tuberculin-tested herds, but obtained from different

dairies. The two girls were not "chums" but attended the same high school.

A check with the school physician revealed that none of the teachers had tuberculosis, with the possible exception of one. She had suffered from pulmonary tuberculosis two years prior, but was discharged from the sanatorium as an arrested case. However, because several of the pupils complained that this teacher coughed during her classes, several sputum examinations were made by the school physician, all of which were found to be negative.

The situation rested at this stage until April, 1937, when a nineteen-year-old girl, graduated from the same high school in 1936, was found to have tuberculosis. Careful inquiry revealed that she had had little or no contact with either of the other girls at the school. She had, however, taken two courses given by the teacher who was under suspicion. An x-ray check-up in her family showed no evidence of active tuberculosis, nor was there any family history of the disease.

Again the evidence pointed to someone in the high school as a potential source of infection for these three girls. The teacher, aware that she was under suspicion, returned to the sanatorium for a check-up. A negative report was received by the school physician from the sanatorium.

In December, 1937, a fourth girl, aged seventeen, was found to have pulmonary tuberculosis. She, too, had had the same teacher in some of her classes. She knew all three of the girls but denied close friendship with them. Her family was examined roentgenographically by a local physician who reported negative findings. Subsequent examination of these films confirmed the original report. At this stage there seemed to be almost overwhelming evidence that these girls had had a common source of infection, and the logical place to search seemed to be in the high school.

Further visits were made to the families to recheck their contact histories. They had all used raw milk from tuberculin-tested herds, but only two of the families took milk from the same dairy. During one of these visits to family C a casual remark opened a new approach to the problem.

It was found that all four families attended the same church. This was a remarkable coincidence. A rough statistical calculation placed the church under strong suspicion on the basis that in the school population considerably less than half a case would be expected to have occurred by chance among this religious denomination if the source of infection were in the school. Inquiries regarding attendance of the girls at the church revealed that three of them sang in the choir and that all four of them had attended social functions on numerous occasions.

A careful check-up of the reported cases and deaths in the community failed to show any of them to be members of this church. However, during the investigations relative to the church membership it was learned, quite by accident, that the wife of the former minister had developed pulmonary tuberculosis and had entered a sanatorium in another state within three months after leaving the parish, early in 1936. This rumor was checked and found to be authentic. In fact, at the time of admission to the sanatorium the minister's wife was found to have tuberculosis in an advanced stage and her sputum was positive.

Further inquiry revealed that the minister's wife also sang soprano in the choir and took communion from a common cup before three of the girls who sang in the choir, as well as before the fourth who was not a choir member. Thus, a common source of infection was found for these four girls in their fellow church member. On the basis of x-ray and sputum examinations and statistics, the schoolteacher, an arrested case, was eliminated from suspicion.

Aside from determining the true source of infection for these four girls, several other factors of epidemiologic significance are manifested. In this particular instance, the range of age was from sixteen to nineteen years and all cases were girls, again revealing the importance of age and sex. However, there is also evidence at the present time to show that the age of highest mortality from tuberculosis is gradually shifting to the older age groups.

A further factor of importance is that three of these girls had positive sputum at the time diagnosis was made; two of them were moderately advanced and two far advanced at the time of diagnosis.

There was a high fatality rate. Two of the girls have died; one remains in a sanatorium; and the fourth has been discharged from the sanatorium as an arrested case.

Although three of the girls sang in the soprano section of the choir, there was ample opportunity for contact between the fourth girl and the minister's wife through social functions and Sunday school. These contacts were regular, usually once or twice a week, over a period of several years.

The question of the common communion cup is a moot one. It is reasonable to suppose that droplet infection through contact at choir practice and social functions might well be sufficient to result in active disease. The dosage of infection was probably large if consideration is given to the cumulative effect resulting from frequent exposures at fairly regular intervals.

Failure to find the source of infection within a household should not preclude further attempts at finding the source case. — Reprinted, in part, from *Tuberculosis Abstracts* (March, 1943).

REPORT OF MEETING

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

A meeting of the Boston City Hospital House Officers' Association was held at the hospital on October 28, 1942. Dr. Edward I. Salisbury, associate director of the Medical Department of the United Fruit Company, spoke on the topic "Malaria."

This disease constitutes the greatest single medical problem of the armed forces in this war. It occurs in all regions in which troops of the United Nations are located, except Greenland and the British Isles. Even Australia has some endemic centers. Although Hawaii has not as yet reported any epidemic, this is almost certain to occur with the transportation of anopheline mosquitoes and their eggs. Mosquito control has been neglected in many regions of this country which are potentially endemic centers for malaria, and disastrous epidemics may result when returning members of the armed forces introduce a new strain of malaria. Anopheline mosquitoes are to be found throughout the extent of both the Atlantic and Pacific seaboards in this country, even to Alaska. There are also centers in the Midwest.

The disappearance of malaria from this country has largely been the result of a movement which has replaced wastelands and swamps with cities. But often ponds have been left for scenic or other reasons, and the fundamental factors for the initiation and spread of an epidemic of malaria are still present. These, then, may be activated by the return of our armed forces, either the wounded during the war or those returning after the war. Even New York and Connecticut have been known to have this disease, whereas Central Europe, especially Russia and the Balkans, are potentially endemic areas.

The prophylaxis employed by the armed forces against this scourge depends on the size of the group under consideration. If small, bed-netting, boots for the ankles and netting over the face when in the field may be used. When the group is large, the need of space for guns and other equipment makes the carrying of large amounts of such paraphernalia impracticable. For the proper carrying out of the recommended suggestions of the Army, each group should have an entomologist and a sanitary engineer.

The Army suggests that during the period when the engineers are improving conditions atabrine be given in doses of 1½ gr. twice a day after meals two days a week, the doses being at least two days apart. Although it is recognized that no drug in safe dosage will prevent mosquito-borne malaria, this drug will suppress fever and decrease the symptoms. Signs and symptoms may develop on withdrawal of atabrine, and the Army advises the staggered withdrawal of the drug in large groups to prevent the mass appearance of malaria. Meanwhile, the entomologist and engineer should attempt to obtain proper conditions at the permanent site of a camp. Drainage of stagnant pools is not always the only thing to do, as evidenced by epidemics in India in which the vector is found only in running water. A capable entomologist will save a great deal of time by tracking down the vector quickly. Different Anopheles have widely divergent habits, some preferring sunny, open streams to the characteristic cool, shady pools.

The treatment of malaria started in the middle of the seventeenth century with the use of the crude bark of the cinchona tree. This was employed until 1820, when the alkaloid quinine was introduced. Quinine has been the drug of choice until quite recently, when several substitutes have been made available.

In 1926, plasmochin, the quiniline derivative of quinine, but obtained from methylene blue, was introduced and was found to be efficacious against *Plasmodium vivax* and the adult form of *P. falciparum*. But it was ineffective in combating the sporulating forms, which cause the clinical manifestations. It is good in combination with quinine, since both the adult forms and the spores are killed.

In 1932 atabrine was developed from a yellow dye. This is effective against the sporulating forms. It is a good substitute for but not equal to quinine. It was formerly employed in relapses, failures to quinine and idiosyncrasies. It is especially good in malaria during pregnancy and in blackwater fever, which seems to be precipitated by quinine. Some authorities decry the use of atabrine with plasmochin, but Dr. Salisbury and many others have used it without mishap for some years. A good seven-day intensive treatment is as follows: 10 gr. of quinine three times a day for three days and 1½ gr. of atabrine for four days; and ⅙ gr. of plasmochin is given three times a day for the last five days.

BOOK REVIEW

Ornithologists of the United States Army Medical Corps: Thirty-six biographies. By Colonel Edgar Erskine Hume, M.C., U.S.A. With foreword by Alexander Wetmore. 4°, cloth, 583 pp., with 109 illustrations. Baltimore: The Johns Hopkins Press, 1942. $5.00.

This volume concerning Army surgeons who were also ornithologists will delight bird lovers and medical historians. In fact it will be a pleasure for all those who are interested in science to read of the remarkable accomplishments of this group. The numerous illustrations—photographs of the ornithologists, some of their drawings of birds and photographs of western Army posts—add much to the interest of the book. It is impossible to mention all the men whose biographies are given in this work. Some of the longer accounts of interest are those of Bendire, Cooper, Elliot, Coues, Mearns, Schufeldt, Casey Wood, Xantus and Yarrow.

Elliott Coues had much to say concerning his friendship with Bendire who confided to him his many trials and tribulations concerning misunderstandings with other ornithologists, particularly Dr. Brewer, and Dr. Coues was able to smooth out many of the troubles and misunderstandings. This resulted in the acquisition by the Smithsonian Institution of Dr. Bendire's large and valuable collection of eggs. In the biography of Coues, due mention is made of his greatest ornithologic works, *Key to North American Birds*, *Birds of the Colorado Valley* and *Birds of the Northwest*. Also, five of his original drawings are reproduced from the *Key*. Dr. Coues also made numerous expeditions for various government surveys. One of his most important works along this line was the account of the Lewis and Clark expedition. He wrote no less than fifteen volumes on his explorations. The biography ends with a touching account of Coues's later life by his great friend Daniel Giraud Elliot.

Edgar Alexander Mearns is one of the most fascinating figures pictured in these biographies. His medical and ornithologic experiences in the Philippine Islands are of extreme interest, as well as his exploration with the Frick Expedition to Africa, when, in less than ten months' time, Dr. Mearns collected fifty-two hundred bird skins. He was a victim of diabetes, unfortunately before the time of insulin, and was in poor health for many years. His energy and enthusiasm under the circumstances were remarkable. Dr. Mearns described and named a large number of birds.

The monumental work of Casey Wood on avian ophthalmology is given due praise in the biography of this famous physician. The exact title of this work was *The Fundus Occuli of Birds, Especially as Viewed by the Ophthalmoscope*. Dr. Wood was a medical historian of note, and the following interesting statement is made in his biography: "Col. Wood's last work or publication is a translation of the famous 'De Arte Venandi cum Avibus,' written in barbaric Latin, a work on medieval ornithology and falconry by the Emperor Frederick II of Hohenstaufen (1194–1250 A.D.)."

Perhaps no work published of late has shown more adequately the selfless interest and devotion to science of such men as these. In the stress and strain of the present time, the book comes to those who are interested in ornithology, medical history and medical science like a fresh summer breeze over a salt marsh. The reviewer believes that it is the most valuable book of its type that has ever been published, and that it will undoubtedly bring great pleasure to its many readers.

NOTICES

JOSEPH H. PRATT
DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM, APRIL

Friday, April 2 — Some Recent Advances in Chemotherapy. Dr. Donald Anderson.
Wednesday, April 7 — Diabetic clinic. Dr. Joseph Rosenthal.
Friday, April 9 — Traumatic Shock. Dr. J. C. Aub.
Wednesday, April 14 — Prevention of Pulmonary Embolism in Thrombosis of the Veins of the Legs. Dr. John Homans.
Friday, April 16 — Modern Conceptions of Poliomyelitis. Dr. Conrad Wesselhoeft.
Wednesday, April 21 — Statistics in the Determination of the L. D. 50 point in bio-assay. Dr. E. B. Wilson.
Friday, April 23 — Comparative Action of Glycosides on the Mammalian Heart. Dr. Gordon Moe.
Wednesday, April 28 — Pediatric clinic. Dr. F. C. MacDonald.
Friday, April 30 — Clinicopathological conference. Dr. Franklin White and Dr. H. E. MacMahon.

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, April 6, at 8:15 p.m. Dr. George W. Thorn will speak on the subject, "High-Protein Diet: Clinical considerations." A discussion by Drs. Frederick J. Stare, William H. Forbes and Robert E. Johnson will follow.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	April 2	Albert H. Brewster
Salem	April 5	Paul W. Hugenberger
Haverhill	April 7	William T. Green
Brockton	April 8	George W. Van Gorder
Worcester	April 16	John W. O'Meara
Pittsfield	April 19	Frank A. Slowick
Northampton	April 21	Garry deN. Hough, Jr.
Fall River	April 26	Eugene A. McCarthy
Hyannis	April 27	Paul L. Norton

WAR CONFERENCE

The American Association of Industrial Physicians, the American Industrial Hygiene Association and the National Conference of Governmental Hygienists will combine their annual meetings in a four-day War Conference at Rochester, New York, on May 24, 25, 26, and 27. The topics to be discussed include the following: the mass entry of women into industry; the placement and employability of aged persons and Class IV*F* rejectees; the rehabilitation and employment of those discharged from the armed services because of disability; the hazards of new substances and processes; absenteeism, fatigue and nutrition; effects of long hours, double shifts and overtime; and the increased rates of industrial accidents.

Physicians, surgeons and all others who are interested

(Notices continued on page xi)

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*A New Type of Medication to Be Used in Bronchial Asthma and Other Allergic Conditions. *New England Journal of Medicine* 223:843–846, 1940

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in the problems of industrial health and their solution are cordially invited to attend; no registration fee is required.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, April 8, at 7 p.m. in the classroom in the nurses' residence. Dr. Edward A. Cooney will speak on the subject, "Management of Burns with Reference to the Role of the Boston City Hospital in the Cocoanut Grove Fire," and will show films. Dr. Felicia A. Banas will be chairman. It should be noted that there has been a change in the usual date and time.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, March 28

Monday, March 29
Annual Massachusetts Safety Conference on War Production and Civilian Defense. Hotel Statler, Boston.
*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, March 30
Annual Massachusetts Safety Conference on War Production and Civilian Defense. Hotel Statler, Boston.
*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, March 31
*9:00–10:00 a.m. Weil's Disease. Dr. Francis E. Bruno. Joseph H. Pratt Diagnostic Hospital.
*12:00 m. Clinicopathological conference. Children's Hospital.
Tufts College Medical School Alumni Association. Dinner, Copley-Plaza Hotel, Boston.

Thursday, April 1
*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

Friday, April 2
9:00–10:00 a.m. Some Recent Advances in Chemotherapy. Dr. Donald Anderson. Joseph H. Pratt Diagnostic Hospital.

Saturday, April 3
*10.00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

April 2–30. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Page ix.
April 5 and 6. Association for the Study of Internal Secretions. Page xi, issue of February 25.
April 6. Greater Boston Medical Society. Page ix.
April 8. New England Hospital for Women and Children. Notice elsewhere on this page.
May 19–25. American Board of Obstetrics and Gynecology. Page xii, issue of March 4.
May 24–27. War Conference. Page ix.
May 25 and 26. Massachusetts Medical Society. Hotel Statler, Boston.
June 4 and 5. American Board of Ophthalmology. Page xii, issue of March 4.

District Societies

BRISTOL SOUTH
May 6. New Bedford.

ESSEX NORTH
May 5.

ESSEX SOUTH
April 7. Addison Gilbert Hospital, Gloucester.
May 5. Salem Country Club.

FRANKLIN
May 11. Annual meeting.
Meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE
May 5.

MIDDLESEX EAST
May 5. Bear Hill Golf Club, Stoneham, 6:30 p.m.

MIDDLESEX NORTH
April 28.
July 28.

PLYMOUTH
April 15. Bridgewater State Farm.
May 20. Lakeville.

WORCESTER
April 4. Hahnemann Hospital, Worcester.
May 12. Annual meeting.

WORCESTER NORTH
April 28.
July 28.

Washingtonian Hospital

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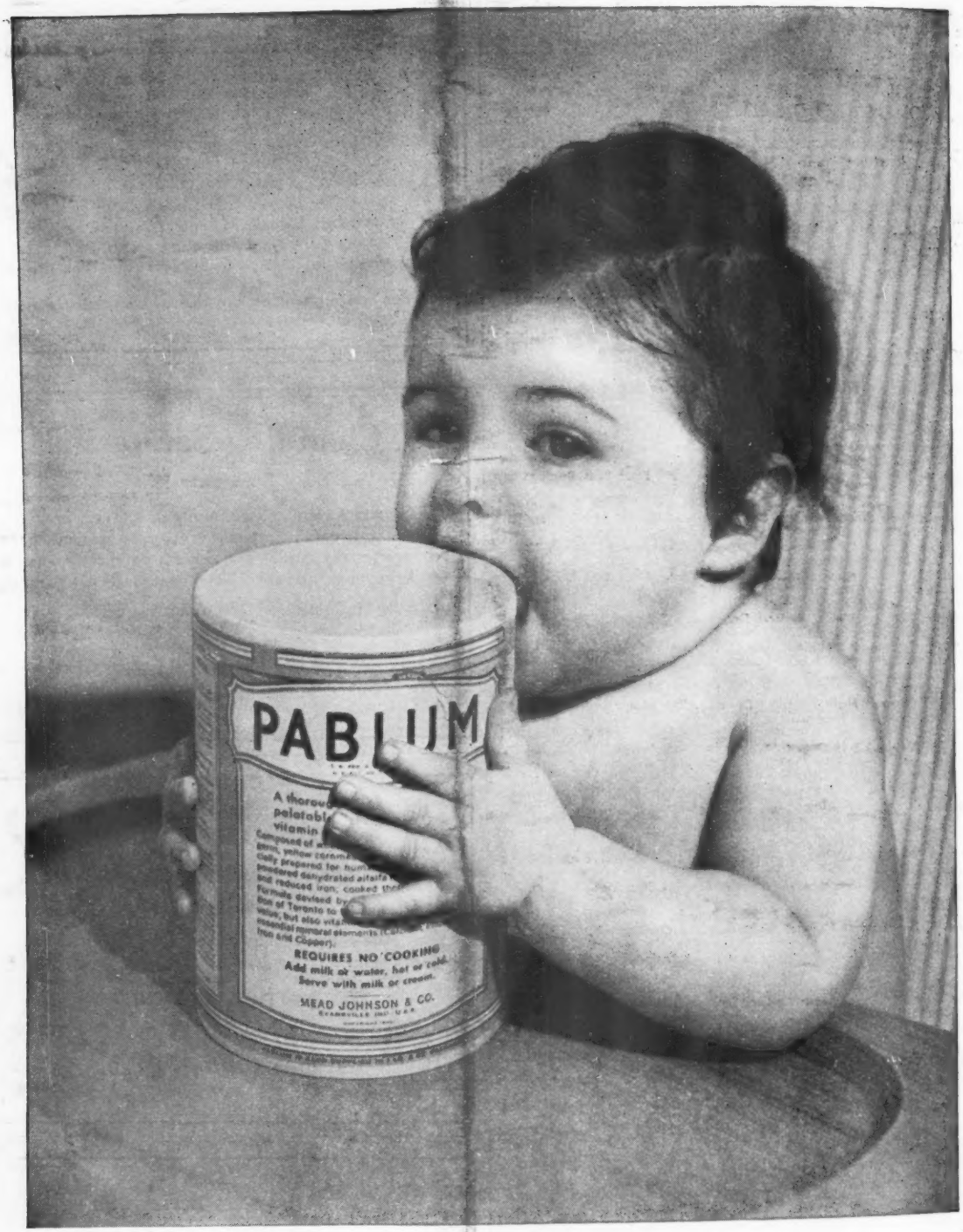

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